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A SPECIALISED COURSE OF PATHOLOGICAL ANATOMY

PART 2

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Unit 14 DISEASES OF GENITAL TRACT AND THE BREST.

Diseases of Pregnancy: Placental polyp; Ectopic pregnancy; Gestational trophoblastic disease and Toxaemia of pregnancy (preeclampsia, eclampsia).

Definition: Ectopic pregnancy is implantation of the fertilized ovum in any site other than normal uterine location: in tubes (tubal pregnancy), in ovaries (ovarian pregnancy), in abdominal cavity (peritoneal pregnancy).

Gestational trophoblastic disease has been divided into three overlapping morphologic categories: hydatidum mole, invasive mole, and choriocarcinoma.

There are 2 subtypes of the hydatidum Mole:

Complete Mole; it never contains fetal parts; all of the chorionic villi are abnormal;

Partial Mole; it contains fetal parts; villous edema involves only some of the villi, and the trophoblastic proliferation is focal and slight.

Diseases of genital tract may be divided into three groups: 1 Inflammative disease;

2 dishormonal diseases; 3 tumors.

Diseases of the uterus: Endocervicosis; Cervicitis; Tumors of the cervix; endometrial hyperplasia; Endometritis; Tumors of the uterus body.

Microsamples:

№ 267 Placental polyp.
№ 204 Ectopic tubal pregnancy design (des).
№ 208 Hydatidiform Mole des.
№ 143 Choriocarcinoma.
№ 209 Endocervicosis des.
№ 75 Endometrial hyperplasia.
№ 129 Fibroadenoma of the breast.
№ 157 Nodular hyperplasia of the prostate

Macrosamples:

Endocervicosis.
Nodular hyperplasia of the prostate.
Leiomyoma of the uterus.

Shortening***: Design- des.*** Hematoxilin and eosin - H & E

Microsamples:

1 № 267 PLACENTAL POLYP H & E

Microscopically: There are placental villi and decidual tissue with necrosis, inflammation and growth of connective tissue.

Definition: Placental polyp is the remainder part of the placental tissue in uterine cavity after abortion or childbirth and results in organization.

Clinical signs are hemorrhage or inflammation.

2 № 204 ECTOPIC TUBAL PREGNANCY H & E ***des***.

Microscopically: There are light decidual cells in the mucosal membrane. One can see blood clots and chorionic villi with syncytial and Langhans cells.

Grossly: the tube is usually locally distended up to 3 to 4 cm by a contained mass of freshly clotted blood bits of grey placental tissue and fetal parts can be seen there.

Etiology: the cause of tubal pregnancy is a tubal pathway obstruction as a result of chronic inflammation, intrauterine tumours, endometriosis and anatomic abnormalities.

Pathogenesis: In all sites, ectopic pregnancies are characterized by fairly normal early development of the embryo, with the formation of placental tissue, the amniotic sac, and decidual changes. An abdominal pregnancy is occasionally carried to term. With tubal pregnancies, however, the invading placenta eventually burrows through the wall of the oviduct, causing intratubal hemorrhage (hematosalpinx), intraperitoneal hemorrhage, or both. Less commonly, poor attachment of the placenta to the tubal wall leads to death of the embryo, with spontaneous proteolysis and absorption of the products of conception.

Types of the disease: Tubal pregnancy is divided into 3 types according to the place of egg implantation:

Ampular tubal pregnancy – if the fertilized egg is implanted in peritoneal part of the tube;

Interstitial tubal pregnancy – if the egg is implanted in the intrauterine portion of the oviduct;

Fimbrial pregnancy – if the egg is implanted in fimbriated end of the oviduct.

Outcome The outcome of the tubal pregnancy is tubular abortion, which may be complete or non-complete. The tubal abortion is characterized by dilacerations of the egg and its movement along the tube.

Complication: In non-complete abortion the egg remains in the tube causing intratubal hemorrhage (hematosalpinx). Sometimes the tube wall

ruptures with intraperitoneal hemorrhage. In complete tubular abortion the egg drops out of the oviduct into abdominal cavity and occasionally may implants on the peritoneum with peritoneal pregnancy development. But as usual the fetus develops calcification (Lithopedion) or mummification (Paper fetus).

Clinical significance: Until rupture occurs, an ectopic pregnancy may be indistinguishable from a normal one, with cessation of menstruation and elevation of serum and urinary placental hormones. Under the influence of these hormones, the endometrium (in about 50% of cases) develops characteristic hypersecretory and decidual changes. However, the absence of elevated gonadotropin levels does not exclude this diagnosis, as poor attachment with necrosis of the placenta is common. Rupture of ectopic pregnancy may be catastrophic, with the sudden onset of intense abdominal pain and signs of acute abdomen, often followed by shock. Prompt surgical intervention is necessary.

Possible cause of death: Abdominal hemorrhage.

3 № 208 HYDATIDIFORM MOLE H & E ***des.***

Microscopically: the Mole shows hydropic swelling of chorionic villi and virtual absence of vascularisation of villi. Stroma is myxomatous and edematous with cysts formation, filled with eosinophillic fluid. Villi are covered by chorionic epithelium, which shows some degree of proliferation of both cytotrophoblast and syncytial trophoblast.

Grossly: uterus is enlarged, the uterine cavity filled with a delicate, friable mass of thin-walled, translucent cystic structures resembling grapes.

Definition: Hydatidiform Mole is a kind of Gestational Trophoblastic Disease manifests itself as a mass of swollen, cystically dilated chorionic villi, covered by proliferating cytotrophoblast and syncytial trophoblast.

Etiology: The disease of unknown etiology. Mole is thought to be a result of ovarian hormonal dysfunction.

Pathogenesis: Two distinctive subtypes of moles are characterized: complete and partial. The complete hydatidiform mole does not permit embryogenesis and therefore never contains fetal parts. All of the chorionic villi are abnormal, and the chorionic epithelial cells are diploid (46, XX or, uncommonly, 46, XY). The partial hydatidiform mole is compatible with early embryo formation and therefore contains fetal parts, has some normal chorionic villi, and is almost always triploid (e.g., 69, XXY). The two patterns result from abnormal fertilization; in a complete mole an empty egg is fertilized by two spermatozoa (or a diploid sperm), yielding the diploid karyotype, while in a partial mole a normal egg is fer-

tilized by two spermatozoa (or a diploid sperm), resulting in the triploid karyotype.

Outcome: In the cases of Mole the fetus either absent, or dying not later than the 4-th month of gestation.

Complication: The Mole is characterized by metrorrhagia in the 1-st trimester of pregnancy. Being diagnosed the Mole needs to be removed from the uterus, as it can become invasive or cause malignisation.

Clinical significance: Overall, 85% of moles remain benign after thorough curettage; 10% of complete moles become invasive, but not more than 2% to 3% give rise to choriocarcinoma. Partial moles rarely give rise to choriocarcinomas. With complete moles, monitoring the postcurettage blood and urine levels of HCG, particularly the more definitive beta subunit of the hormone, permits detection of incomplete removal or a more serious complication and leads to administration of appropriate therapy, including in some cases chemotherapy, which is almost always curative.

Possible causes of death: Endometrial hemorrhage, amniotic embolism of lungs.

4 № 143 CHORIOCARCINOMA. H & E

Microscopically: It is composed of atypical anaplastic cuboidal cytotrophoblast and syncytiotrophoblast. The stroma is absent.

Grossly: choriocarcinoma shows extremely hemorrhagic, necrotic masses within

the uterus.

Definition: It is a malignant tumor derived from the placenta.

Clinical signs: Metastasizes early and widely. Primary focus may disintegrate, leaving only metastases within the lung, vagina, brain, liver and kidney.

5 № 209 ENDOCERVICOSIS H & E ***des.***

Microscopically: Columnar epithelium of “cervical” type appears in the vaginal portion of the cervix instead of squamous cell epithelium, which is present in normal condition. Multiple endocervical glands are observed well down the cervical wall.

Grossly: Endocervicosis is noted as reddening, swelling, and granularity around the margins of the external cervical os.

Definition: Endocervicosis is a dishormonal disease, characterized by the presence of endocervical glands in the vaginal portion of the cervix.

Etiology: The disease is thought to result from 1) chronic inflammation (chronic cervicitis), which may show metaplastic pattern in repair; 2) dis-

hormonal changes in pregnancy or ovarian dysfunction; 3) mechanical rupture of the cervix, for example as complication of the childbirth (ectropion).

Pathogenesis: Endocervicosis is considered by many of scientists to be the result of normal changes in adult women. Remodeling occurs continuously with regrowth of the squamous epithelium up to the original external os. The area replaced by the squamous epithelium is known as the transformation zone. Frequently, overgrowth of the regenerating squamous epithelium blocks the orifice of endocervical glands in the transformation zone to produce small nabothian cysts lined by columnar mucus-secreting epithelium.

Types of the disease: Endocervicosis is divided into 3 types to show the stages of the disease at the same time. Proliferative endocervicosis; Simple endocervicosis;
Regenerating endocervicosis.
There are 3 histological variants of endocervicosis: Papillary; Glandular; Mixed.

Outcome: Endocervicosis as usual leads to epidermization (regrowth of squamous
epithelium).

Complication: Endocervicosis is extremely common associated with inflammation, both non-infectious and infectious. Endocervicosis was thought in the past as a background process disease of the cervical carcinoma.

6 №75 ENDOMETRIAL HYPERPLASIA H & E.

Microscopically: Architectural structure of endometrium is damaged; the difference between the basal and superficial parts of endometrium is not clear; the glands are increased in number and can show some cystic pattern. In cases of complex hyperplasia nests of closely packed glands appear, accompanied by intensive cell proliferation. Atypical hyperplasia shows cell atypism.

Grossly: Endometrium is thickened with some polypoid prominences.

Definition: Endometrial hyperplasia is a dishormonal disease, closely related to estrogen excess, characterized by intensive cell proliferation, accompanied by increasing number of glands and some stromal disorders in endometrium.

Etiology: Any basis for estrogen excess may lead to hyperplasia. Failure of ovulation, such as is seen in menopause; prolonged administration of estrogenic steroids without counter-balancing progestin; estrogen-

producing ovarian lesions such as polycystic ovaries (including Stein-Leventhal syndrome); cortical stromal hyperplasia; granulose-theca cell tumours of the ovary.

Types of the disease: Endometrial hyperplasia is divided into 3 types: Simple hyperplasia, Complex adenomatous hyperplasia, atypical hyperplasia.

Outcome and complications: Endometrial hyperplasia causes excessive and
irregular uterine bleeding.

Clinical significance: Atypical hyperplasia shows some risk of progressing within 20% - 25% to adenocarcinoma of the endometrium. It is evident that when atypical hyperplasia is revealed, it must be carefully evaluated for possible presence of a focus of cancer, and must be continuously monitored by repeated endometrial biopsy to evaluate its course.

7№ 129 FIBROADENOMA OF THE BREAST.
See above in epithelial derived tumors part.

8 № 157 NODULAR HYPERPLASIA OF THE PROSTATE H & E

Synonyms: 1) Benign prostatic hypertrophy, and 2) Dishormonal hyperplasic prostatopathy.

Microscopically: The hyperplasic nodules are composed of varying proportions
of proliferating glandular elements and fibromuscular stroma.

Grossly: Prostate is enlarged, projecting into the bladder lumen, with hypertrophy of the bladder wall. The cut surface of prostate contains numerous nodules of different sizes, of solid or cystic appearance.

Definition: It is a dishormonal disease, characterized by proliferation of both epithelial and stromal elements of the prostate, with resultant enlargement of the gland, and in some cases, urinary obstruction.

Types of the disease: according to predominance of proliferation of glands or stroma, the nodular hypertrophy of the prostate is divided into 3 histological types Glandular, Stromal, and Mixed.

Complication and clinical significance: In severe cases hypertrophied prostate may project into the bladder lumen, causing urethral obstruction, leading to difficulty in urine voiding. Under this condition the bladder wall shows hypertrophy.

This process is not complete and often accompanied by residual urine in the bladder.

The risk of urinary tract infection increases, including sepsis and Hydronephrosis.

Macrosamples:
Leiomyoma of the uterus.
See above in mesenchymal derived tumors part.

UNIT15 ENDOCRINE DISEASES

The thyroid gland may be enlarged and named goiter or struma.

Macroscopic classification as follows: diffuse, nodular and mixed.

Microscopic classification as follows: colloidal, parenchymatous and mixed.

Clinical classification follows: euthyroid (normal function), hypothyroid (decreasing function) and hyperthyroid (increasing function).

Diseases occur as endemic goiter, sporadic goiter, diffuse toxic goiter (Basedov's
disease, Grave's disease).

Endemic goiter occurs in geographic areas where soil, water and food supply contain low levels of iodine. Morphologically it is a diffuse non-toxic goiter, colloid goiter.

Sporadic goiter occurs in most cases when the cause is not evident. Morphologically it is diffuse or nodular non-toxic colloid goiter.

Diffuse toxic goiter (Basedov's disease, Grave's disease) is an autoimmune disease with production of antibodies to TCG-receptors. It is a diffuse, toxic goiter with follicles hyperplasia, mixed goiter.

Goiter may occur as Hashimoto's thyroiditis or Riedel's thyroiditis.

Endocrine pancreas consists of the islets of Langerhans with general part of B-cells to produce insulin.

Diabetes mellitus is a clinical syndrome or geterogenous disease characterized by absolute or relative insufficiency of insulin with chronic disorder of carbohydrates, fat, and protein metabolism and hyperglycemia as a common symptom.

There are Type 1 and type 11 diabetes.

Type 1 is characterized by β-cells destruction. Etiology: genetic transformation, virus infections, and nutrition factors, toxic substances .Pathogenesis: Primary destruction β-cells. There are Changes of antigens on the surface of β-cells. Then one can see insulinitis, and secondary autoimmune and idiopathic lesions of β-cells.

Morphology: there is an inflammation (insulinitis) of the islands with lymphocytes
and macrophages infiltration with dystrophy of β-cells.
Type 11 is characterized by primary relative insufficiency of insulin with insulin resistance.

Etiology: genetic prediabetes, obesity, hypodynamia, overeating, starvation, stress.

Pathogenesis: Primary insulin resistance, primary dysfunction of β-cells and etiologic factors leading to hyperglycemia, hyperinsulinemia, secondary insulin resistance, relative deficit of insulin, secondary dysfunction of β-cells, atrophy of the pancreas, absolute deficit of insulin.

Morphology: there are atrophy islands, sclerosis and lipomatosis of the stroma.
Diabetic micro and macro angiopathy:

Microangiopathy: there are proliferation and desquamation of the endothelium, plasma infiltration, lipohyalinosis and sclerosis of the arterioles and small arteries, with thickening of the basic membranes.

Macroangiopathy: it is manifested by atherosclerosis with many vascular involvements with rapid progression and frequent thromboses.
In Diabetic nephropathy one can see glomerulopathy (sclerosis and hyalinosis of the glomeruli) and tubulopathy (vacuole and hyaline droplet dystrophy).
In Diabetic neuropathy: one can see thinning and sclerotic epineuron, edema and dystrophy of nerve fibers. Diabetic ophthalmopathy.

Consequences: Diabetic comas, gangrene of leg and foot, chronic renal failure,
blindness.
Pituitary consists of adenohypophysis (anterior pituitary), and neurohypophysis (posterior pituitary).
In most of the cases, excess production of anterior pituitary hormones is caused by presence of an adenoma arising in the anterior pituitary.
Basophilic-cell adenoma (corticotropinoma) may cause hypercortisolism as Icenko -Cushing disease with excessive production of adrenocorticotrophic hormone (ACTH).

Clinical manifestations include hypertension, weight gain (truncal obesity), decreased muscle mass, hyperglycemia, glucosuria, polydipsia, hirsutism, osteoporosis, menstrual abnormalities, and mental disturbances.

Eosinophilic-cell adenoma (somatotropinoma) may cause disease named Acromegaly to follow with excessive production of somatotrophic or growth hormone (GH).

Clinical manifestations include conspicuous irregular growth in soft tissues, skin,
and viscera, in the bones of the face, hands, feet and jaws.
Hypofunction of anterior pituitary with GH deficiency during Childhood leads to disease of pituitary dwarfism with growth failure.

Causes of GH deficiency: necrosis, hemorrhage, inflammation, radiation, tumours.

Adrenal cortex synthesizes and secretes steroid hormones: glucocorticoids, mineral corticoids and adrenocortical androgens.
Excessive hormone levels with hyperadrenalism leads to Cushing syndrome,
hyperaldosteronism, and virilizing syndromes.

Hypoadrenalism or adrenal insufficiency occurs as primary Hypoadrenalism divided into chronic and acute.
Chronic primary adrenal insufficiency is termed Addison disease.

Addison disease is an uncommon disorder resulting from progressive destruction of the adrenal cortex.

Causes include autoimmune adrenalitis, infections, tuberculosis, metastatic neoplasm and amyloidosis.

Clinical signs follow: Hyperpigmentation of the skin and the mucosal surfaces,
gastrointestinal disturbances, hyperkalemia, hyponatremia, volume depletion and
hypotension.

Hyperpigmentation is caused by increasing of melanin production. Adrenal hormone deficiency and increased level of ACTH precursor hormone stimulate
melanocytes.

Adrenocortical adenomas are benign tumours. They are classificated by hormonal activity and cytogenesis. Aldosteroma is derived from zone glomerulosa with clinical manifestation of Conn syndrome; Corticosteroma is derived from zone fasciculate with clinical manifestation of Cushing syndrome; Androsteroma is derived from zone reticularis with clinical manifestation of adrenogenital syndromes.

Parathyroid glands synthesize and secret parathyroid hormone (PTH), which in its turn activates osteoclasts, thereby mobilizing calcium from bone. The renal tubular reabsorbtion 0f calcium increases
The conversion of vitamin D to its active dihydroxy form in the kidneys increases.

Urinary phosphate excretion increases. Augment of gastrointestinal calcium absorption occurs.

Parathyroid adenoma with hyperparathyroidism leads to parathyroid osteodystrophy or parathyroid osteosis (Recklinghausen'sdisease) with an increase in the level of serum ionized calcium and hypophosphataemia.

Clinical signs include OSTEOPOROSIS, OSTEITIS FIBROSA CISTICA, FRACTURES, NEPHROLITHIASIS, POLIURIA, GALLSTONES, and PEPTIC ULCER.

Microsamples:
1 № 277 Colloidal goiter des.
2 № 278 Basedow's goiter des.
3 № 279 Colloidal goiter with local Basedow's goiter
4 № 54 Glycogen accumulation in renal tubular epithelium see 1-st se mester
5 № 281 Basophilic adenoma of the pituitary gland
6 № 292 Bones with parathyroid osteodystrophy des.
7 № 280 Adenoma (corticosteroma) of the adrenal gland

Macrosamples:
1 Goiter (Struma)
2 Gangrene of the foot see 1-st semester
3 Atrophy of the pancreas
4 Obesity of the subcutaneous fatty tissue see 1-st semester
5 Myocardial hypertrophy see 1-st semester
6 Bones with parathyroid osteodystrophy
7 Skin with Addison's disease

Microsamples:

1№ 277 COLLOIDAL GOITRE (DIFFUSE AND MULTINODULAR GOITRE) H& E **des**

Microscopically: The follicular epithelium may be hyperplasic in the early stages of disease and flattened or cuboidal during periods of involution. Colloid is abundant during the latter periods.

Grossly: The cut surface of the thyroid is usually brown, glassy, and translucent. It may be smooth or hilly.

Definition: Diffuse or focal enlargement of the thyroid gland is termed goiter.

Classification: Colloid goiter may be diffuse and nodular non-toxic goiter.

Result is shown in regressive changes (areas of fibrosis, hemorrhage, calcification, cystic changes).

Clinical signs: The degree of thyroid enlargement is proportional to the level and duration of thyroid hormone lack. In most cases the increased thyroid mass achieves a euthyroid state but in some cases hyperthyroidism occurs.

(Thyrotoxicosis) or hypothyroidism may result.

2 № 278 DIFFUSE TOXIC GOITRE (Basedov's disease, Graves's disease) H & E ***des***

Microscopically: There are diffuse hypertrophy and hyperplasia of thyroid follicular epithelial cells. They are tall, columnar and more crowned than usual, with formation of small papillae which project into follicular lumen. The colloid within the follicular lumen is pale with scalloped margins, lymphoid infiltrates of predominantly of T cells with fewer B cells and mature plasma cells present throughout the interstitium, germinal centers are common.

Grossly: The thyroid gland is diffusely enlarged, smooth, and soft, its capsule is intact.

Microscopical picture of the extrathyroid changes:

There is generalized lymphoid hyperplasia is evident. Ophthalmopathy is caused by oedematous orbital tissues with presence of hydrophilic glycosaminoglycans and infiltration by lymphocytes, mostly T cells. The heart muscles may be hypertrophic with serous myocarditis to result in sclerosis. The liver may be with serous inflammation and lymphocyte infiltration to result in sclerosis and rarely cirrhosis. The derma thickening due to deposition of glycosaminoglycans and lymphocyte infiltration is shows.

Clinical signs: 1 thyrotoxicosis (tachycardia, heart failure, ophthalmopathy (proptosis or exophthalmia);

2 Serum TSH concentrations are decreased; 3 increase of free T4 and T3.

Causes of death: 1 heart failure; 2 liver failure; 3 cahexia; 4 acute adrenal insufficiency with total thyroid ectomy to follow.

3 № 281 BASOPHILIC ADENOMA OF THE PITUITERY GLAND H & E. (Corticotrophin cell adenoma)

Microscopically: Pituitary anterior basophilic adenoma consists of uniform polygonal cells with supporting connective tissue or reticulin.

Grossly: Pituitary adenoma is a well circumscribed soft, small tumor (less than 2cm).

Disease is termed ***Icenko – Cushing's disease*** with increase of adrenocorticotrophic hormone (ACTH) and hypercortisolism.

Clinical signs: 1 hypertension; 2 weight gain ("buffalo hump"); 3 decreased muscle mass; 4 hyperglycemia; 5 glucosuria; 6 polydipsia; 7 coetaneous striae; 8 hirsutism; 9 osteoporosis.

4 № 292 BONES WITH PARATHYROID OSTEODYSTROPHY H&E ***des***

Microscopically: Changes include prominence of osteoclasts, which are in turn erode bone matrix and mobilize calcium salts, particularly, in the metaphases of long tubular bones. Bone resorption is accompanied by increased osteoblastic activity and the formation of new bone trabeculae. The marrow contains increased amounts of fibrous tissue accompanied by foci of hemorrhage and cyst formation.

Grossly: Bones with parathyroid osteodystrophy occurs in the form of "brown tumor of hyperparathyroidism''. Bones become soft, with multiple tumor-like formations of multicolored structures with red-brown and yellow-grey locations.

Definition: Hyperparathyroidism is a disease that results from disorders intrinsic to the glands to produce autonomous hypersecretion of parathyroid hormone leading to hypocalcaemia and hypophosphataemia. These changes are accompanied by osteodystrophy, nephrocalcinosis and gastrointestinal alterations.

Etiology: Adenoma or primary hyperplasia of the parathyroid glands.

Clinical signs: The elevated levels of parathyroid hormone induce a number of changes, including excessive bone resorption, hypercalcemia and renal diseases.

5№ 280 ADENOMA (CORTICOSTEROMA) OF THE ADRENAL GLAND H&E

Microscopically: There are cortical adenoma consists of light cells with mild nuclear pleomorphism.

Grossly: It is a well- circumscribed node with the adrenal capsule expansion. It is small in size, 1 to 2cm in dm, of yellow or yellow-brown color.

Definition: Corticosteroma is a benign tumor derived from the cells of the adrenal zone fasciculate.

Classification: 1 Light cell adenoma consists of vacuolated cells, rich in lipids, with formed alveolar structures; 2 Dark cell adenoma consists of

cells with homogenous eosinophilic cytoplasm, formed trabeculae and tension bars.

Clinical signs: The tumor may produce glucocorticoids. Clinical syndrome is termed Cushing's syndrome with severe derangement of fatty exchange.

Macrosamples:

Atrophy of the pancreas

Grossly: One can see atrophy of the islands and parenchyma with stromal sclerosis and lipomatosis of the pancreas.

The disease is termed diabetes mellitus 11 type.

Clinical signs are as follows: Hyperglycemia, hyperinsulinemia, and deficit of insulin to follow.

Skin in Addison's disease

Grossly: There are skin and mucosal surfaces with hyperpigmentation. The adrenals are reduced to small, flattened structures usually retaining their yellow color with atrophy of cortical zone and intact medulla.

Definition: Addison's disease is chronic adrenal insufficiency resulting from progressive destruction of the adrenal cortex.

Etiology: Autoimmune adrenalitis, tuberculosis, acquired immunodeficiency syndrome, metastasis, systemic amyloidosis, fungal infections, hemochromatosis, sarcoidosis.

Clinical signs: Gastrointestinal disturbances, hyperpigmentation of the skin, hyperkalemia, hyponatremia, volume depletion, hypotension.

Death develops rapidly unless corticosteroids are replaced immediately.

Unit16 RHEUMATIC DISEASES. VALVULAR HEART DISEASES. CONGENITAL HEART DISEASES.

Definition: Rheumatic diseases are diseases with systemic disorganization of the connective tissue.

Classification: There are: rheumatism, rheumatoid arthritis, systemic lupus erythematosus, systemic scleroderma, periarteritis nodosa, and dermatomiositis.

The most common diseases are Rheumatism, Systemic lupus erythematosus, Periarteritis nodosa.

Definition: Rheumatism is autoimmune disease with systemic disorganization of the connective tissue with predominance destruction of the cardiovascular system.

Classification: Clinical morphologic forms: cardiovascular; arthritic; cerebral;
nodosal.

Etiology: Rheumatic fever is a disease that develops, a few weeks after, an episode of β- hemolytic group A streptococcal pharyngitis. It does not cause infections by similar streptococci at other sites, such as skin. Fortunately, rheumatic fever occurs only in about 3% of patients with β-hemolytic group A streptococcal pharyngitis. However, after an initial attack, increased predisposition to reactivation of the disease follows with subsequent pharyngeal infections.

There are stages of disorganization of the connective tissue: mucoid and fibrinoid
swelling.

Pathogenesis: The pathogenesis of acute rheumatic fever and its chronic sequel a is not fully understood. It is strongly suspected that acute rheumatic fever is a hypersensitivity reaction induced by group A streptococci. It is proposed that antibodies directed against the M proteins of certain strains of streptococci cross-react with tissue glycoproteins in the heart, joints, and other tissues. The onset of symptoms is within 2 to 3 weeks after infection and the absence of streptococci from the lesions support the concept that rheumatic fever results from an immune response against the of fending bacteria. Its nature of cross-reacting antigens is difficult to define, it has also been suggested that the streptococcal infection evokes an autoimmune response against self-antigens.

The course of Rheumatism may be acute, subacute, lingering, and latent.

Active phase of Rheumatism is termed Rheumatic fever.

Rheumatic fever is an acute, immunological mediated, multisystem inflammatory disease, predominantly affecting cardio-vascular system, characterized by recurrent episodes of acute phase alternating with remission.

There are rheumatic pericarditis, myocarditis, endocarditis, carditis (myocarditis and endocarditis) and pancarditis.

Clinical features related to acute carditis include pericardial friction rubs, weak heart sounds, tachycardia, and arrhythmias. Chronic rheumatic carditis usually does not cause clinical manifestations for years or even decades after the initial episode of rheumatic fever.

Rheumatic pericarditis may be serous or fibrinous (“Hair heart”) to develop synechii, obliteration of the pericardial cavity or calcification
into the formed connective tissue (“stone [shell] heart”)

There are 3 types of Rheumatic myocarditis:

1Granulematous Rheumatic myocarditis (Nodular proliferative); 2 Diffuse exudative interstitial; 3 Local exudative interstitial.

Diffuse exudative interstitial myocarditis is characterized by edema, hyperemia and prominent chronic mononuclear infiltration of myocardial stroma. Granulomas are not characteristic for this type of myocarditis.

Grossly the heart is flabby, its chambers are dilated. Decompensation develops frequently, leading to death of patient. Local exudative interstitial myocarditis is characterized by insignificant local mononuclear cell infiltration of myocardium. Granulomas are not common. This type of myocarditis is characteristic for latent Rheumatic fever.

Morphologic evidence of endocarditis is as follows:

Endocarditis is an inflammation of endocardium. *It is divided* into 3 types: valvular, chordal and mural. However, in rheumatic fever, inflammation tends to be most pronounced in the mitral and aortic valves. The affected valves are oedematous and thickened.

Histological signs are as follows: dystrophies and necrobiosis of endothelium, mucoid and fibrinoid swelling and fibrinoid necrosis of connective tissue, cell proliferation (granulomatosis) and thrombus formation can be revealed. This morphologic feature may show different combinations.

4morphologic types of rheumatic valvular endocarditis are established. They are:

1Valvulitis, that is diffuse endocarditis, characterized by dystrophic changes in valvular connective tissue without affecting endothelium thrombus formation.

2 Verrucous endocarditis. The inflammation of the valve leads to endothelium injury and predisposes to the formation of small vegetations, particularly along the lines of valve closure.

3 Fibroplastic endocarditis. It develops as a result of acute progressive changes and characterized by significant scarring.

4 Recurrent verrucous endocarditis, that is repetitive disorganization of connective tissue, accompanied by endothelium injury and thrombus formation on the background of sclerosis and thickening of the valve.

Polyarteritis nodosa

Polyarteritis nodosa is another common rheumatic disease.

Definition: Polyarteritis nodosa is a disease of medium-sized to small arteries that is characterized by Transmural acute necrotizing inflammation of these vessels.

Etiology: Polyarteritis nodosa is a disease of unknown etiology and may be viruses of hepatitis B, C, cytomegalovirus, HIV-infection may contribute.

Pathogenesis: The leading role in pathogenesis is that of immuno-complex mechanism of vessel wall injury, resulting in fibrinoid necrosis. *Morphologic* evidence can be seen in kidneys, heart, liver, and gastrointes tinal tract, with pancreas, testes, skeletal muscle, nervous system, and skin to be involved.

Classification: 1 Destructive vasculitis (fibrinoid necrosis); 2 Proliferative-destructive vasculitis (lympho-plasmacytes infiltration with sclero sis); 3 Proliferative vasculitis.

Outcome: Sclerosis of the vascular walls.

Complication: thrombosis; rupture of the vascular walls and hemorrhages; infarctions.

Valvular Heart diseases.

Definition: They are significant structural changes of the heart with intracranial and systemic blood supply disturbance.

Classification: Stenosis orifice and regurgitation (insufficiency) aortic, mitral valves are distinguished. They are compensated and decompensate. They can be multivalvular disease (mitral- aortal valves disease) and combined stenosis with regurgitation.

Congenital heart diseases (Malformation valve diseases)

Ventricular and atrial septal defects, Patent ductus arteriosus, ***Tetralogy of Fallot***

(Dextraposed aorta, Ventricular septal defect, Narrowed pulmonary ar***tery,*** Hypertrophied right ventricle).

Microsamples:

1 № 174 Recurrent verrucous endocarditis des.
2 № 178 Valvular scleroses.
3 № 177 Granulematous rheumatic myocarditis des.
4 № 81 Fibrinous pericarditis. See Exudative inflammation 1 semester.
5 № 36 Mucoid swelling of the cardiac valve.
6 № 310 Kidney in polyarteritis nodosa des.

Macrosamples:

1 Ischemic infarctions of the spleen. See 1-st semester
2 Mitral stenosis.
3 “Haired heart”. See 1-st semester
4 Recurrent verrucous endocarditis

5 Ventricular septal defect.
6 “Nut meg” liver. See 1-st semester
7 Brown induration of the lung. See 1-st semester

Microsamples:

1№ 174 RECURRENT VERRUCOUS ENDOCARDITIS H & E ***des.***

Microscopically: The valve shows prominent fibrosis, which can be accompanied by hyalinosis, and even Calcium deposition. At the same time, dystrophic changes such as mucoid and fibrinoid swelling are usually observed, which can cause fibrinoid necrosis of connective tissue. Sometimes Aschoff- Talalayev’s nodules appear. The inflammation of the valve predisposes to the formation of thrombotic masses on the endothelium.

Grossly: Affected valves are fibrous thickened with solid consistency. Small vegetations, seen as wart like excrescences, are visible along the line of closure of the valve leaflet.

Features described beyond are characteristic of Rheumatic Fever and Heart Disease.

Outcome: Rheumatic endocarditis results in sclerosis and hyalinosis of endocardium, leading to thickening of the valve and chronic irreversible valvular deformities.

Clinical correlations and complications:

Signs and symptoms of valvular disease depend on which cardiac valve or valves are involved. In addition to various cardiac murmurs, cardiac hypertrophy and dilation, and congestive heart failure, patients with chronic rheumatic heart disease may suffer from arrhythmias, thromboembolic complications, and infective endocarditis.

2№ 178 VALVULAR SCLEROSES. H& E

Microscopically: scarring with valvular deformities occurs.

Grossly: They are thick, rigid, and interadherent valve leaflets and chordae tendineae.

Result is formation of mitral stenosis or regurgitation.

2 № 36 MUCOID SWELLING OF THE CARDIAC VALVE. Toluidin blue stain.

Microscopically: There is a mucoid swelling region of crimson color of within valve leaflet called metachromasia. It is the first change of leaflet tissue in acute rheumatic fever.

Result is fibrinoid swelling and sclerosis formation.

3 № 178 VALVULAR SCLEROSES. H& E

Microscopically: Scaring with valvular deformities occurs.

Grossly: They are thick, rigid, and interadherent valve leaflets and chordae tendineae.

Result is formation of mitral stenosis or regurgitation.

4 № 177 GRANULOMATOUS RHEUMATIC MYOCARDITIS H & E ***des.***

Microscopically: multiple foci of inflammation within the connective tissue of the heart, termed Aschoff- Tallalaev's bodies, are revealed. They contain a central focus of fibrinoid necrosis, surrounded by a chronic mononuclear inflammatory infiltrate, and occasional large histiocytes with vesicular nuclei and abundant basophilic cytoplasm, termed Anitschkow cells. Aschoff- Talalayev's bodies may be found anywhere in the connective tissue of the heart, but most common they are in the left ventricular auricular region. In the myocardium, they often lie in close proximity to a small vessel and may encroach on its wall. In addition to Aschoff- Talalayev's bodies, the myocardium may also contain diffuse interstitial inflammatory infiltrates.

Grossly: In severely affected cases, the myocarditis may result in generalized dilation of the cardiac chambers and perivascular cardiosclerosis.

Definition: Myocarditis – is an inflammation of the heart muscle (from Greek terms: mayor – muscle, and cardis – heart, plus suffix "itis", meaning inflammation).

Etiology and pathogenesis (see description beyond)

Morphologic evidence of myocarditis is as follows:

Granulematous myocarditis is characterized by appearance of numerous small granulomas (Aschoff bodies) within connective tissue of the heart. Most of them are localized in the left ventricular auricular, posterior wall of the left ventricle, and ventricular septa. There are 2 phases of granulomas development: 1) Mature granulomas present in acute phase of Rheumatic fever (attack), and 2) Sclerosing granulomas – in remission phase.

Outcome: Diffuse and perivascular cardiosclerosis leading to chronic heart insufficiency. Generalized dilation of the cardiac chambers with decompensation of hypertrophied myocardium leading to acute heart insufficiency.

5 №310 KIDNEY IN POLIARTERITIS NODOSA H & E ***des.***

Microscopically: Transmural inflammation of the arterial wall with heavy infiltrate of neutrophils, eosinophils, and mononuclear cells, accompanied by fibrinoid necrosis of the inner half of the vessel wall. Occasionally aneurismal dilation can be observed. The lumen is thrombosed. At the same time chronic fibrous thickening of the vessel wall is present.

Complication: In kidney subacute (extracapillary productive) or chronic (mesangial) glomerulonephritis usually develops leading to nephrosclerosis and progressive renal insufficiency.

Clinical correlations: Renal involvement is one of the prominent manifestations of the disease and major cause of death. Hypertension is common and may precede inherent renal disease. Manifestations are so diverse that clinical diagnosis often needs to be established by biopsy of suspected areas of involvement, with sites being affected are kidney and skeletal muscle.

Macrosamples

Recurrent verrucous endocarditis

Grossly: Small vegetations are visible along the line of closure of the mitral valve leaflets with fibrous thickening and fusion of valve leaflets. See above.

Mitral stenosis

Grossly: Valve leaflets and chordae tendineae are thick, rigid, and interadherent. The mitral orifice is narrowed to a slit like channel.

Definition: reduction in the diameter of the mitral valve orifice is termed stenosis.

Cause: Chronic rheumatic mitral valvulitis results in the valve leaflets scarring,

Classification: mitral stenosis is sometimes designated as "fish-mouth" or “diaphragm” deformity.

Complication: The left atrium is dilated and hypertrophied, and the endocardial surface is often thickened, particularly above the posterior mitral leaflet. Mural thrombi may be present, revealing a potential source of systemic emboli. The lungs are firm and heavy as a result of chronic passive congestion, and in advanced cases the right ventricle and atrium are dilated and hypertrophied as well.

Clinical sign: It occurs more frequently in females than in males, reasons remain unclear.

Ventricular septal defect.

Grossly: It may involve any part of the interventricular septum.

Cause: Ventricular septal defect develops within the fourth and eighth weeks of gestation.

Pathogenesis: It is formed by the fusion of an intraventricular muscular ridge.

Clinical sign: Ventricular septal defect is a cyanotic clinical form of malformation of the heart. It is the most common congenital heart defect at birth.

Unit 17 ATHEROSCLEROSIS. ISCHEMIC HEART DISEASE.

Atherosclerosis is a chronic disease with the lipid and protein abnormal metabolisms and destruction of the large aorta and arteries (elastic type and myoelastic types) with the formation of atherosclerotic (fibrofatty) plaques.

Manifestation of the atherosclerosis is in Atherosclerotic plaque.

Forms of atherosclerosis: 1) cerebral and carotid arterial injury (as cerebrovascular disease); 2) cardiac arterial injury (ischemic heart disease); 3) renal arterial injury;

4) injury of the aorta; 5) injury of the intestinal arteries; 6) injury of the extremity arteries.

Clinical signs are in development of Atherosclerosis into other diseases of the principal organs. Myocardial infarction is a form of ischemic heart disease with development of myocardial necrosis area caused by the local insufficiency of blood supply.

Ischemic heart disease refers to a group of closely related diseases caused by imbalance between myocardial oxygen demand and blood supply.

Microsamples

1 160b Atherosclerotic plaque (atheroma) des.

2 162b Transmural myocardial infarct with organization des.

3 163 Large area of postinfarction myocardial fibrosis (as cardiosclerosis).

Macrosamples

1 Atherosclerosis of the aorta with mural thrombus in the aorta.

2 Gangrene of the foot (see 1 semester)

3 Gangrene of the intestine (see 1 semester)

4 Ischemic infarct of the spleen (see 1 semester)

5 Ischemic infarct of the heart with acute aneurism
6 Chronic aneurism of the heart

Microsamples

1 160b ATHEROSCLEROTIC PLAQUE (ATHEROMA) H&E ***des.***

Microscopically: one can observe the intimal thickening with cell migration,
proliferation and extracellular matrix elaboration in the intimae.

Atherosclerotic plaque has three principal components: 1) cells (smooth muscle cells, macrophages, other leukocytes);
2) extracellular matrix (collagen, elastic fibers, proteoglycans);
3) intra- and extra cellular lipid.
All components can be seen within the fibrous cap of the plaque.
The necrotic center consists of cell debris, cholesterol crystals, foam cells and calcium.

There are two types of atherosclerotic plaques: 1 vulnerable plaques; 2 stable plaques.

Grossly: Aorta demonstrates multiple fatty and fibrous plaques, some of them with diffuse and complicated lesions (calcinosis, ulceration, thrombosis).

There are ***six stages*** of atherosclerotic plaques: 1) prelipidosis; 2) lipidosis;
3) atheromatosis; 4) ulceration; 5) sclerosis; 6) calcinosis.
Complication of the atherosclerotic plaque: 1) calcinosis; 2) ulceration; 3) rupture with hemorrhage; 4) thrombosis; 5) aneurismal dilatation; 6) embolism (thromboembolism and fatty embolism).
Clinical significance according to the complications: 1 atherosclerotic plaque occludes lumina of blood flow compromise to distal parts of organs and cause
ischemic injury. Thrombi, thromboemboli and fatty emboli may also obstruct
blood flow too. 2 aneurisms may rupture with hemorrhage.

Causes of death: 1) rupture with hemorrhage; 2) thrombo- and fatty embolism with occlusion of the lumina blood flow compromise of the principal organs.

№ 162b TRANSMURAL MYOCARDIAL INFARCTION WITH STATING ***OF*** ORGANISATION H&E ***des***.

Microscopically: the cardiac muscle cells are bright and eosinophilic, due to coagulate necrosis. The myocardial cells may show contraction bands. Nuclei are absent.

Within10 days after the event necrotic myocytes at the periphery of the infarct are replaced by granulation (as young connective) tissue with numerous macrophages remnants (debris) of necrotic myocytes.

Definition: Infarct as the pathologic process is an area of ischemic necrosis within a tissue or an organ produced by occlusion of its arterial supply.

The causes of the infarct are 1) thrombus; 2) embolus; 3) atherosclerotic plaque;

4) prolonged spasm.

There are three stages of infarct progression: 1 ischemia; 2 necrosis 3 sclerosis(as the formation of the scar).

There are four forms of infarct according to the left wall thickness:

1) subendocardial; 2) transmural; 3) intramural; 4) subepicardial.

The result is sclerosis (formation of the scar).

Complication: 1 rupture of the infarct; 2 mural thrombi; 3 acute fibrinous pericarditis; 4 papillary muscle dysfunction; 5 ventricular aneurysms (acute and chronic).

Causes of death: 1) cardiac arrhythmias; 2) left ventricular failure; 3) cardiac shock; 4) rupture of the wall, the septum or the papillary muscle; 5) thromboembolism.

3 № 163 LARGE AREA OF POSTINFARCTION MYOCARDIAL FIBROSIS

(AS CARDIOSCLEROSIS) H&E.

Microscopically: One can see extensive myocardial fibrosis with atrophic and hypertrophic myocardial cells surrounding fibrosis. Myocardial fibrosis is the form of chronic ischemic heart disease (termed sometimes ischemic cardiomyopathy).

Classification: There are small and large scars, single or multiple, diffuse as atherosclerotic cardiosclerosis.

Etiology:1) myocardial infarct.

Complication: 1) compensatory heart failure; 2) chronic decompensatory heart failure; 3) acute heart failure with pulmonale edema.

Causes of death: 1 chronic decompensatory heart failure; 2 acute heart failure with pulmonale edema; 3 arrhythmias.

Macrosamples

Atherosclerosis of the aorta with mural thrombus in it.

Grossly: Mild atherosclerosis composed of fibrous plaques, severe one may be seen with diffuse and complicated lesions including mural mixed thrombus.

Result is thromboembolism.

Ischemic infarct of the heart with acute aneurism

Grossly: The zone of infarct is a pale, firm, fairly well-defined region with a hyperemic border. The aneurysm is visible as a thin-walled pouching out of the ventricular wall.

Result is rupture of the aneurism with hemopericardium.

Cause of death may be cardiac [pericardial] tamponade.

Chronic aneurism of the heart

Grossly: The necrotic myocardium is completely replaced by dense whitish scar tissue with a thinned area as a chronic aneurism in the left ventricular myocardium.

Complication: Thromboendocarditis may be in zone of a chronic aneurism with thromboembolism.

Unit 17 ARTERIAL HYPERTENSION. HYPERTONIC DISEASE. CEREBROVASCULAR DISEASE.

Hypertonic disease.

Definition: Hypertonic disease as Primary or essential arterial hypertension is the chronic disease with high constant arterial pressure when the relationship between blood volume and total peripheral resistance is altered.

The secondary forms of artery hypertension occur as the symptom of other diseases. Their causes are well understood.

The forms of hypertonic disease are as follow: 1 cerebral; 2 cardiac; 3 renal.

1 cerebral form consists of cerebrovascular disease with hemorrhages or ischemic infarctions. 2 cardiac form consists of ischemic heart disease. 3 renal form consists of arteriolosclerosis and primary wrinkled or contracted kidneys followed by azotemia or uremia.

The stages of arterial hypertension are as follow: 1) functional; 2) changes of the vessels; 3) changes within the organs.

There are benign and malignant arterial hypertensions. Benign hypertension has

major morphologic characteristic as hyaline and sclerosis of the arterioles and small arteries, especially with renal form of arterial hypertension.

Malignant hypertension has morphologic characteristics as necrotizing arteriolitis and hyperplasic arteriolosclerosis, particularly in kidneys.

Causes of death: 1 cardiac insufficiency; 2 uremia; 3 hemorrhage or ischemic infarction of the brain.

Microsamples:

1 N 167 The vessels of the brain with hypertonic disease (arterial hypertension) des.
2 N 73 Hypertrophy of the myocardium (see 1 semester)
3 N 16a Hemorrhage in the brain (see 1 semester)
4 N 166 Arteriolosclerotic nephrosclerosis des.

Macrosamples:

1 Hemorrhage in the brain (see 1 semester)
2 Hypertrophy of the myocardium (“cow heart”) (see 1 semester)
3 Fatty degeneration of the myocardium (see 1 semester)
4 Nephrosclerosis (“primary wrinkled [contracted] kidney”)

Microsamples:

1 N 167 THE VESSELS OF THE BRAIN WITH HYPERTONIC DISEASE (PRIMARY ARTERIAL HYPERTENTION) H&E ***des.***

Microscopically: one can see small muscular arteries and arterioles with acute changes: 1 fibrinoid necrosis of the wall; 2 high permeability of the wall; 3 hemorrhages; 4 aneurysm; with chronic changes: 1 hyalinosis; 2 scle roses; 3 narrowing of the lumen.

Grossly: one can observe only hemorrhages and sclerosis with narrowing of the vascular lumen. Sometimes aneurism can be noted.

Definition: Hypertonic crisis rapidly increases in arterial hypertension with lesions of the organs, especially within the brain.

Clinical signs: neurological disintegration.

Causes of death: hemorrhage or ischemic infarction of the brain can be revealed.

2 N 166 ARTERIOLOSCLEROTIC NEPHROSCLEROSIS. H&E ***des.***

Microscopically: there are fields of sclerosis within renal stroma, glomeruli may
occur in sclerosis or hyalinosis, but process of sclerosis and hyalinosis of

the small muscular arteries and arterioles is evident. Their lumen is narrow.

Arteriolosclerosis and hyalinosis of the arterioles and small arteries are signs of benign arterial hypertension within kidney.

Hyperplastic arteriolosclerosis, necrotizing arteriolitis and glomeruloli tis are the morphologic signs of malignant arterial hypertension

Grossly: Kidneys are small, contracted with granular surface.

Result is nephrosclerosis as primary wrinkled or contracted kidneys.

Clinical signs and cause of death: chronic renal failure (uremia).

Unit 18 RENAL DISEASES

Glomerular diseases consist of Primary and secondary glomerulonephritis and Nephrotic syndrome.

Primary glomerulonephritis is a disease where kidney is the only or predominant organ involved. *Secondary glomerulonephritis* is a disease where glomeruli can be injured in the course of a number of systemic diseases. They can be Immune diseases such as systemic lupus erythematosus (SLE) and amyloidosis; vascular disorders such as arterial hypertension and polyarteritis nodosa; metabolic diseases such as diabetes mellitus.

Primary glomerulonephritis is a disease with immune mediated inflammation of glomeruli and lesion of both kidneys with renal and extra renal symptoms.

Renal symptoms are as follows: haematuria, proteinuria, oliguria and casts in urine. *Extra renal symptoms* are as follows: azotemia, hyperglobulinemia, disproteinemia, hypertension, hyperlipidemia, and edema.

Glomerulonephritis can be acute, subacute and chronic with renal tissue reaction to follow.

Acute glomerulonephritis is a disease with acute inflammative lesion of the glomeruli: a) Acute post streptococcus glomerulonephritis; b) acute non streptococcus glomerulonephritis.

Clinical signs: ***nephritic syndrome*** (haematuria, azotemia, mild hypertension, red blood cell casts, oliguria).

Subecute glomerulonephritis is a group of diseases with rapid and progressive decrease of renal functions.

Clinical signs: nephritic syndrome.

Chronic glomerulonephritis is a heterogenic group of renal diseases with different etiology, pathogenesis and course.

Morphologic forms are as follows: a) mesangioproliferative; b) mesangiocapillary; c) fibroplastic;

In final stage of chronic glomerulonephritis, grossly kidneys are symmetrically contracted and have a fine- grained surface *(secondary contraction of the kidneys).*

Clinical sign is uremia (chronic renal failure).

Nephrotic syndrome is a clinical complex, including the following: 1 massive
proteinuria (daily loss in the urine more than 3,5g of protein); 2 hypoalbuminemia; 3generalized edema; 4 hyperlipidemia; 5 lipiduria.

Diseases with Nephrotic syndrome are as follows: a) membranous nephropathy, b) lipoid nephrosis (minimal change disease), c) focal segmental glomerulosclerosis, d) membranoproliferative glomerulonephritis.

All diseases complicated with glomerulopathy always progress to uremia.

Tubulo-intestinal diseases are characterized by primary lesion of tubules and interstitium of the kidney.

Pyelonephritis is a disease with inflammation involving stroma, calyx and pelvis of the kidney. It can be unilateral or bilateral, acute and chronic.

Acute Pyelonephritis is a common suppurative inflammation of the kidney and the renal pelvis caused by bacterial infection.

Pathogenesis: There are two routes for bacteria to reach the kidney: 1 from the lower urinary tract (ascending infection); 2 through the bloodstream (hematogenous);

Ascending infection is the most important and common route for bacteria to affect the kidney.

Etiology: Escherichia coli, Proteus, Klebsiella, Enterobacter, Pseudomonas. The first step appears to be adhesion of bacteria to mucosal surfaces, followed by colonization of distal urethra. From here the organisms must gain access to the bladder, moving against the flow of urine. This may occur during urethral instrumentation (catheterization and cystoscopy).

The background diseases are: 1 urinary tract obstructions (benign prostatic hypertrophy, uterine prolapse); 2 reflux (vesicoureteral or intrarenal); 3 pregnancy; 4 diabetes mellitus.

Hematogenous spread is far less common of the two. *Etiology*: staphylococci and streptococci.

Diseases: Sepsis, Infective endocarditis.

Lesion of the kidney includes suppurative necrosis or abscess formation within stroma, rupturing into tubules, glomeruli, vessels causing sclerosis of the stroma and parenchyma.

Complications are as follows: 1 urogenic sepsis; 2 necrotizing papillitis; 3 suppurative paranephritis; 4 pyonephrosis; 5 apostematous nephritis.

Result is recovery or chronic pyelonephritis.

Chronic Pyelonephritis is termed chronic tubular and interstitial inflammative disease with compatibility of asymmetric, irregular sclerosis and deformation of calyxes and adjacent parenchyma.

It can be divided into two forms: 1) chronic obstructive Pyelonephritis; 2) chronic

Reflux-associated Pyelonephritis.

Morphologic Stages of chronic Pyelonephritis are as follows:

1 atrophy of the ducts, lymphoid infiltration of the stroma;

2 hyalinosis of some of glomeruli; atrophy of ducts with enlarged lumen, filled with colloid mass; sclerosis and lymphoid infiltration of the stroma;

3 hyalinosis of most of glomeruli; ducts with epithelium atrophy, filled with colloid mass (“thyroid” kidney); sclerosis of the stroma, glomeruli, vessels. 4 Severe decrease of cortical tissue, sclerosis of the kidney (“secondary contracted kidneys”) as pyelonephritic contraction of the kidney.

Result is chronic renal failure (uremia) when two kidneys are damaged.

Acute and chronic renal failure

Acute renal failure signifies acute suppression of renal function.

Etiology includes the following: 1 shock; severe Glomerular diseases (rapid progressive glomerulonephritis); 2 crush-syndrome; 3 exogenic intoxication; 4 endogenic intoxication; 5 acute drug –induced interstitial nephritis; 6 incompatible blood transfusion;

Pathogenesis consists of: 1 ischemic renal injury is characterized by severe hemodynamic alterations that cause reduction of the Glomerular Filtrate Rate (GFR); 2 tubular epithelial cells are particularly sensitive to hypoxia and also vulnerable to toxins. This leads to redistribution of membrane proteins (K-Na ATP-ase) resulting in increased sodium delivery to distal tubules. Through a tubuloglomerular feedback system, it causes vasoconstriction and GFR decrease;

The clinical stages are as follows: 1 initiation stage; 2 maintenance (oliguria);

3 polyuria; 4 recovery.

Chronic renal failure (CRF) is the final outcome of a variety of renal diseases and is the major cause of death of renal disease.

There are three stages of CRF:

1 diminished renal reserve [the Glomerular Filtrate Rate (GFR) is 50% of normal, blood urea nitrogen and creatinine values are normal];

2 renal insufficiency (the GFR is 20% to 50% of normal, azotemia appears, polyuria, nocturia occur); 3 Renal failure as uremia (the GFR is less than 20% to 25% of normal; edema, metabolic acidosis, hypocalcemia).

Uremia is azotemia associated with a constellation of clinical signs and symptoms with biochemical abnormalities including uremic gastroenterocolitis, neuropathy, and uremic fibrinous pericarditis.

Azotemia is a biochemical abnormality that refers to an elevation of blood urea nitrogen and creatinine levels.

Grossly the kidneys are symmetrically or nonsymmetrical contracted and their surfaces are red-brown and diffusely granular or hilly.

Microsamples

1 № 192a Acute exudative proliferative intracapillary glomerulonephritis (poststreptococcal)
2 № 193 Rapidly progressive (crescentic) glomerulonephritis ***des.***
3 № 194 Chronic glomerulonephritis with contraction of the kidneys ***des.***
4 № 4 Necrotic nephrosis ***des.***
5 № 196a Chronic Pyelonephritis ***des.***
6 № 44 Amiloid nephrosis (see 1 semester)

Macrosamples

1 Glomerulonephritis (large mottled kidney)
2 Hypertrophy of the left ventricular myocardium (see 1 semester)
3 Nephrosclerosis (“contracted” kidney)
4 Amiloid nephrosis (“lardaceous” kidney) (see 1 semester).
5 The kidney with mechanical jaundice.
6 Hydronephrosis.
7 Apostematous nephritis.
8 Polycystic kidneys.
9 Fibrinous pericarditis (see 1 semester).

Microsamples:

1№192a ACUTE EXUDATIVE PROLIFERATIVE INTRACAPILLARY
GLOMERULONEPHRITIS (poststreptococcal) H&E.

Microscopically: The most characteristic change is a fairly uniformly increased cellularity of the Glomerular tufts that affects nearly all glomeruli. The Increased cellularity is caused both by proliferation and

swelling of endothelial and mesangial cells and by a neutrophilic and monocytic infiltrate.

Electron microscopically: shows the immune complex arrayed as subendothelial, intramembranous or often subepithelial “humps” nestled against the Glomerular basement membranes (GBM). The deposits contain IgG and complement.

Etiology: immune complex formation.

Definition: It is a diffuse proliferative glomerulonephritis with nephritic syndrome development.

Results are recovery, rapidly progressive glomerulonephritis or chronic renal diseases.

Clinical course: Nephritic syndrome may occur with moderate oliguria, azotemia, hypertension, gross haematuria, and proteinuria.

2 № 193 RAPIDLY PROGRESSIVE (CRESCENTIC) GLOMERULONEPHRITIS H &E ***des***.

Grossly: kidneys are enlarged and pale with petechial hemorrhage on surface.

Microscopically: formation of distinctive crescents can be seen. Crescents are formed by proliferation of parietal cells and by migration of monocytes into

Bowman’s space, sometimes with multinucleated giant cells. The crescents eventually obliterate Bowman’s space and compress the glomeruli.

Electron microscopically: may disclose subepithelial deposits and distinct ruptures

in basement membrane (BM).

Etiology: Type 1 anti- GBM antibodies with deposits of IgG and C3 lines on the GBM. Type 2 immune complex mediated disorder. Type 3 pauci-immune type GN.

Definition: It is a clinical syndrome and not a specific etiologic form of GN with clinical picture of rapid and progressive loss of renal function associated with severe oliguria and death from renal failure within weeks to months.

Result is scarring of the glomeruli with formation of the secondary contracted kidneys.

Clinical signs: The onset shows nephritic syndrome and proteinuria approaching nephritic range may occur.

3 № 194 CHRONIC GLOMERULONEPHRITIS WITH SECONDARY CONTRACTED KIDNEY H&E ***des.***

Microscopically: the feature common to all cases is advanced scarring of the glomeruli and complete replacement by hyaline. There are marked interstitial fibrosis, sclerosis of the vessels and duct atrophy.

Grossly: the kidneys are symmetrically contracted and their surfaces are grey – brown and diffusely granular.

Definition: This is the final stage of many glomerulonephritis as secondary contracted kidneys.

Clinical signs: Without treatment the prognosis is poor. Progression to uremia and death is usual.

4 № 4 NECROTIC NEPHROSIS H&E ***des.***

Microscopically: Tubular necrosis (toxic etiology leads to necrosis of proximal tubules with BM spared and ischemic necrotic nephrosis leads to necrosis of shot segments of straight proximal and ascending thick limbs).

Grossly: the kidney is enlarged, swollen, cortex is pale and medulla is hyperemic.

Definition: it is a clinic pathologic entity characterized morphologically by destruction of tubular epithelial cells and clinically by acute suppression of renal function (acute renal failure).

Pathogenesis: 1 persistent and severe disturbances in blood flow; 2tubular injury;

Clinical signs: oliguria, creatinine and blood urine nitrogen increase.

5 № 196a CHRONIC PYELONEPHRITIS H&E ***des.***

Microscopically: changes are largely nonspecific, and similar alteration may be seen with other tubulointerstitial diseases. Interstitial fibrosis and proliferative inflammation with lymphocytes, plasma cells, dilation or contraction of tubules with atrophy of the epithelium can be seen. Many of dilated tubules contain pink casts that suggest the appearance of thyroid tissue, the so-called “thyroidization” of tubules. The wall of the calyces and pelvis are filled with fibrosis and cells of proliferative in flammation.

Grossly: One or both kidneys may be involved, diffusely or in patches. They are not equally damaged and contracted.

Definition: chronic Pyelonephritis is a disease with interstitial inflammation and scarring and inflammation of the pelvicalyceal system.

Etiology: congenital abnormalities of the urethra, calculi with obstruction of low collecting urinary system; reflux (vesicoureteral and intrarenal).

Classification: according to etiology chronic Pyelonephritis occurs as 1 chronic obstructive Pyelonephritis; and 2 chronic reflux-associated Pyelonephritis.

Result is in scarring with formation of secondary contracted kidneys.

Clinical signs: Chronic renal failure, uremia to bilateral lesion follows.

Macrosamples:

Polycystic kidneys.

Grossly: The kidney is markedly enlarged with numerous dilated cysts.

Etiology: 1 autosomal dominant and recessive polycystic Kidney diseases;
2 associated with atherosclerotic Nephrosclerosis; 3 dialysis-associated acquired
cysts.

Hydronephrosis.

Grossly: marked dilation of the pelvis and calyces and thinning of renal parenchyma.

Definition: Hydronephrosis refers to dilation of the renal pelvis and calyces, with accompanying atrophy of the parenchyma, caused by obstruction to urine outflow.

Etiology: 1 congenital (atresia of the urethra); 2 acquired (calculi, necrotic papillae, tumors, inflammation, neurogenic with paralysis of the bladder; normal pregnancy.

Complication: pyonephrosis.

Nephrosclerosis (“contracted” kidney)

Grossly: The kidneys are markedly reduced with rough or granulated surface, solid of grey color.

Etiology: all renal diseases lead to secondary contracted kidney. Diseases of renal vessels lead to primary contracted kidneys.

Clinical signs: chronic renal failure.

Unit 19 DISEASES OF THE LIVER
(Hepatosis, Hepatitis, Cirrhosis and Tumors)

Hepatosis is injuring of the liver with predominance of degeneration (dystrophy) and necrosis of hepatic parenchyma. Hepatosis may be acute and chronic.

The example of acute Hepatosis is Massive hepatic necrosis.

Result is postnecrotic cirrhosis or death.

The example of chronic Hepatosis is Hepatic steatosis (fatty liver). This is a reversible disease after course of treatment. Another result is hepatitis.

Hepatitis

Definition: Hepatitis is a disease connected with injury of hepatocytes associated with an influx of inflammatory cells into the liver.

Etiology: Continuous infections of viral hepatitis; alcoholism, drugs, Wilson's disease.

The classifications are as follow: 1a) primary hepatitis; b) secondary hepatitis.

Primary hepatitis is an original disease. Secondary one develops with other diseases.

2 a) acute; b) chronic.

Primary hepatitis according to etiology: a) viral; b) alcoholic; c) autoimmune; d) drug-induced.

Viral hepatitis: 1) acute may be: HAV, HBV, HCV, HDV, HEV, and HGV; 2) chronic may be: HBV, HCV, HDV, HEV, HGV (excluding HAV).

Pathogenesis of hepatitis B : 1 *acute infection*: a) 60% subclinical disease; b) 25% acute hepatitis; c) 10% " healthy" carrier; d) 5% persistent infection; Subclinical disease –100% recovery; acute hepatitis –99% recovery & 1% fulminant hepatitis and death. Persistent infection 90% recovery and 10% chronic hepatitis. *Chronic hepatitis*- 50% cirrhosis and death; cirrhosis 10% -hepatocellular carcinoma.

Acute hepatitis: *Grossly* the liver is enlarged, of red color. *Microscopically*: 1) hydropic and ballooning cell degeneration; b) bridge and piecemeal necrosis; c) apoptotic bodies (Councilman bodies); d) infiltration of portal and lobular stroma with lymphocytes, macrophages, some granulocytes; e) proliferation of reticuloendoteliocytes; g) cholestasis; h) regeneration of the hepatocytes.

The right markers of HBV infection are "ground –glass" hepatocytes with HbsAg; "sanded" nuclei with HbcAg.

Clinical morphologic forms of acute viral hepatitis lead to a) cyclic jaundice; b) without jaundice; c) fulminant; d) cholestatic.

Results of acute viral hepatitis are: a) recovery; b) acute hepatic and renal failure with death; c) chronic hepatitis; d) cirrhosis.

Chronic hepatitis: *etiologic Classification is as* follows: 1 viral; 2 autoimmune; 3 medical; 4 cryptogenic.

Classification according to activity is as follows:

1 hepatitis with minimal activity and mild activity (persistence); 2 hepatitis with moderate and severe degrees of activity (aggressive).

Classification according to stage: 0 –absence of fibrosis; 1- flabby fibrosis; 2- moderate fibrosis; 3- severe fibrosis.

Microscopical picture of chronic hepatitis B: Hydropic and balloon dystrophies; *Councilman's bodies* are as apoptotic bodies; necrotic hepatocytes; Lymphomacrophageal infiltration; Hyperplasia and proliferation of Kupffer cells; Fibrosis of periportal tracts.

Cirrhosis

Definition: Cirrhosis is the chronic disease of the liver, characterized by fibrous septa bridging, parenchymal nodules (pseudolobules) and disruption of the architecture of the entire liver.

Classifications: are as follows: 1) *according to etiology* a) infectious; b) toxic (alcoholic); c) toxic-allergic; d) biliary; e) metabolic-alimentary; e) discirculatory; g) cryptogenic.

2) *according to morphology*: a) macronodular; b) micronodular; c) mixed.

3) *according to* morphogenesis: a) portal; b) postnecrotic; c) mix.

4) *according to* character of course: a) active; b) nonactive.

Clinical signs: portal hypertension, hemorrhage from varicose veins of the esophagus and hepatocellular failure as *the causes of the death.*

Portal hypertension demonstrates varicose veins of the esophagus, abdomen and hemorrhoid veins; ascites, congestive splenomegaly, hepatic encephalopathy, skin spider angioma.

Hepatocellular failure demonstrates jaundice, encephalopathy, hepatorenal syndrome, coagulopathy, hypoalbuminemia, endocrine disorders.

Hepatargia is the clinic syndrome developing with severe hepatorenal failure or hepatic intoxication and exhibited neuropsychic dysfunction and potential hepatic coma.

Cirrhosis complications: hepatic coma, hemorrhage out of esophagus varicose veins, ascites and peritonitis, thrombosis of the portal vein, hepatocellular carcinoma.

Result is death of patient.

Microsamples:

1 № 202 Massive hepatic necrosis (toxic dystrophy of the liver) des.

2 № 314 Chronic nonactive (persistence) hepatitis des.

3 № 200 Portal cirrhosis des.

4№ 313 Chronic active (aggressive) hepatitis with piecemeal necrosis

5 № 203 Biliary cirrhosis of the liver

6 № 312 Alcoholic steatosis of the liver

Macrosamples:
1Massive hepatic necrosis (as toxic dystrophy of the liver)
2 Hepatic cteatosis (Fatty liver) see first semester
3 Cirrhosis of the liver
4 Nutmeg liver, see first semester
5 Pigmental cirrhosis (as hemachromatosis disease) see first semester
6 Verrices of the esophagus (see first semester)

Microsamples:
1 № 202 MASSIVE HEPATIC NECROSIS (TOXIC DYSTROPHY OF THE LIVER) H & E ***des.***

Microscopically: the structure of the liver is destroyed with necrosis of the hepatocytes. Only a collapsed reticulin framework and preserved portal tracts may occur. There are a lot of macrophages and new connective tissue. The regenerative hepatocytes can be seen.

Grossly: the liver is smaller than normal, shrink, soft, of red, yellow color and spotted and with wrinkled capsule.

Definition: Massive hepatic necrosis is an acute Hepatosis with necrosis of hepatocytes.

Etiology: 1) exogenic agents (mushroom, arsenic, heliotrope, phosphorus, drugs); 2) endogenic intoxications (gestosis, thyrotoxicosis);
3) viral hepatitis (fulminate forms).

Morphological stages: 1-st week – fatty) of the hepatocytes into lobular centers. The liver is smaller than normal, soft, of yellow color.
2-d week – yellow stage. Necrosis within lobules occurs.
3-th week – red degeneration (dystrophy) stage. The resorption of fatty-protein detritus with naked hyperemic sinusoids, collapse of the stroma, the liver is of red color.

Results are hepatic or hepatic renal failure as a cause of death or may be postnecrotic macronodular cirrhosis of the liver.

Clinical signs: Fulminant hepatic failure with clinical hepatic insufficiency progressing to hepatic encephalopathy.

2 № 314 CHRONIC MILD ACTIVE (PERSISTANCE) HEPATITIS H & E ***des.***

Microscopically: portal tracts expanded by lymphocytic, macrophages infiltration with occasional plasma cells and rare neutrophils or eosino-

phils can be seen, but no extension into parenchyma and necrosis of a few liver cells. Normal lobular formation is retained.

Definition: This is a form of chronic hepatitis with smoldering hepatocytes necrosis and inflammation, limited to portal tract.

Etiology: 1viral; 2 alcoholic; 3 autoimmune; 4 drug-induced.

Pathogenesis: there is Cross-reaction of immune cell sensibilization with antigens can be observed as antigens of hepatocytes look like antigens of virus.

Results are recovery or fibrosis of periportal tracts or very rare in cirrhosis.

3 № 313 CHRONIC WITH SEVERE ACTIVE (AGGRESSIVE) HEPATITIS (WITH PIECEMEAL NECROSIS) H& E

Microscopically: Lymphomacrophageal infiltrate extends from the portal tract into the parenchyma, causing progressive destruction of hepatocytes ("piecemeal" necrosis and bridge necrosis);

"ground –glass" hepatocytes with HbsAg; "sanded" nuclei with HbcAg. Bridge necrosis leading to cirrhosis may occur.

Result is small nodular (portal) cirrhosis.

4 № 200 PORTAL CIRRHOSIS H&E ***des***.

Microscopically: Hepatocellular necrosis, replacement fibrosis and inflammation, vascular derangement and hyperplasia of surviving liver tissue as pseudolobules. Fibrous septa dissect and surround nodules.

Grossly: The liver may be enlarged or reduced, firm, with a micronodular surface, of gray and yellow colors.

Definition: Portal cirrhosis is the final and irreversible form of alcoholic liver disease usually evolving slowly and insidiously. Portal cirrhosis may be the final form of viral liver disease.

Morphogenesis: the developing fibrous septa are delicate and extend through sinusoids from central vein to portal regions and from portal tract to portal tract; regenerative activity of parenchymal hepatocytes generates fairly uniformly sized nodules. These nodules tend to be less than 0,3 cm in dia, this pattern of cirrhosis is termed micronodular cirrhosis.

Causes of death may be hepatic failure, massive esophagus hemorrhage, intercurrent infection, hepatorenal syndrome, hepatocellular carcinoma.

5 № 203 BILIARY CIRRHOSIS OF THE LIVER H & E

It may be 1) primary; 2) secondary.

Definition: Primary biliary cirrhosis is rare chronic cholestatic inflammative disease with autoimmune reactions to follow.

Secondary biliary cirrhosis is chronic disease with extrahepatic bile duct obstruction to follow.

Microscopically: prominent bile stasis in bile ducts, bile duct proliferation with surrounding neutrophils, portal tract edema. Periportal fibrosis with nodular formation can be seen.

Grossly: the liver is smaller than normal, firm, of green color.

Etiology: Biliary atresia, gallstones, stricture, carcinoma of pancreas head.

Clinical signs: Pruritus, hepatic and infrahepatic jaundice, malaise, dark urine, light stools, hepatosplenomegaly.

Result is death of patient.

6 № 312 ALCOHOLIC STEATOSIS OF THE LIVER. H&E and Sudan three

Fatty liver or steatosis of the liver may be as the first stage of the alcoholic diseases. Alcoholic disease evolves to Steatosis- hepatitis- portal cirrhosis.

Microscopically: one can see micro and macrovacuoles within the hepatocytes; they are of yellow color with "Sudan three".

Grossly: the liver is enlarged, of yellow color, soft. It is the so-called "goose liver".

Definition: Fatty liver is a chronic Hepatosis with predominance of fatty degeneration (dystrophy) within the hepatocytes.

Result is recovery or chronic hepatitis.

Unit 20 DISEASES OF GASTROINTESTINAL TRACT.
DISEASES OF GALLBLADDER.

Ulcerous disease

Definition: ulcerous (peptic ulcerous) disease is a chronic disease in clinical cyclic course and its morphologic appearance is chronic recidivate ulcer of the stomach or duodenum.

Classification: 1 ulcer of the gastric body; 2 ulcer of the pyloroantral region; 3 ulcer of the pyloroduodenal region.

Etiology: 1 Helicobacter pylori; 2 imbalance of neural regulation; 3 disturbance of hormonal regulation; 4 lesions of acid peptic regulative factors; 5 destruction of glandular apparatus.

Pathogenesis: General and local factors of ulcer development occur.

General factors consist of hormonal and nervous abnormalities of regulation of gastroduodenal system. Local factors of ulcer pathogenesis consist of various abnormalities of balance between aggressive factors of gastric acid and pepsin and protection of gastric mucosal membrane.

Morphogenesis: there are stages of chronic ulcer formation: 1 acute erosion; 2 acute ulcer; 3 chronic ulcer.

Complication: 1 perforation, 2 peritonitis, 3 penetration, 4 bleeding, 5stenosis, 6 malignisation, 7 combinations of complications.

Cholecystitis

Definition: cholecystitis is a disease with an inflammation of the gallbladder wall.

Classifications: 1 calculous and aculculous cholecystitis.
2 acute and chronic.

Classification of Acute cholecystitis is as follows: 1 catarrhal; 2 suppurative: a) phlegmonous; b) phlegmonous and ulcerate; c) apostematous; 3 fibrinous (diphtheritic); 4 gangrenous.

Classification of Chronic cholecystitis is as follows: 1 atrophic; 2 hypertrophic.

Etiology: 1infection may be as follows a) enterogenic; b) hematogenic; c) hepatogenic; 2 circulation disturbance within gall bladder.

Cholelithiasis

Definition: holelythiasis is a disease with formation of bile stones.

Classification: bile stones are cholesterol, pigment, calcic and mixed stones.

Appendicitis

Appendicitis is a disease with inflammation of the appendix.

Classification is as follows 1 acute; 2 chronic.

Acute appendicitis is revealed as simple, superficial, phlegmonous, phlegmonous and ulcerous, gangrenous and apostematous.

Complications of acute appendicitis are as follows:
1 perforation; 2 suppurative peritonitis; 3 periappendicular abscess; 4 empyema;
5 pyleflebitis; 6 abscesses of the liver.

Chronic appendicitis occurs as a result of acute simple and superficial appendicitis.

There can be seen growth of granulate tissue and formation of scar with obliteration of the appendicular lumen.

Complications of chronic appendicitis are as follows:
a)hydrocele;b)mucocele; d)myxoglobulosis.

Microsamples
1 № 264 Erosions of the stomach
2 № 266 Chronic ulcer of the stomach des.
3 № 76 Phlegmonous cholecystitis des
4 № 77 Chronic cholecystitis.
5 № 263 Phlegmonous ulcerous appendicitis des
6 № 270 Mucocele

Macrosamples
1 Chronic ulcer of the stomach
2 Phlegmonous appendicitis
3 Gangrenous appendicitis
4 Calculous cholecystitis
5 Choledoch stone (common bile duct)

Microsamples

1 № 264 EROSION OF THE STOMACH H&E

Microscopically: The local mucous membrane of the stomach is destroyed and covered with the fibrinous film and leukocyte infiltration. There are acute erosions.

Etiology see chronic ulcer. Erosions can be with hemorrhagic gastritis and the first stage of the chronic ulcer.

Erosion results are 1 healing; 2 formation of ulcer.

2 № 266 CHRONIC ULCER OF THE STOMACH. H&E. ***des***

Microscopically: The wall of the stomach is destroyed within some area and formation of crater.

The bottom of ulcerous defect is covered by fibrinous mass and leukocytes (1), Underline by a zone of fibrinoid necrosis (2), underline by granulation tissue (3), Depth is a fibrous, calagenous scar (4).

Vessels with fibrinoid necrosis trapped within the scarred area are thickened walls and occasionally thrombosed.

Grossly: The ulcer is a defect of the wall; mostly are round, sharply punched-out craters of 2 to 4 cm in dia. Preferred site is lesser curvature of the stomach.

Etiology: the ulcer is induced by imbalance between the gastroduodenal Mucosal defenses and the countervailing aggressive forces to overcome such defenses: a) aggressive forces: 1 mucosal exposure to gastric acid and pepsin; 2 extremely strong causal association with *H. Pylori infection;* 3 aggravating forces: aspirin, cigarettes, alcohol, impaired regula-

tion of acid- pepsin secretion. b) impaired defenses: ischemia, shock, delayed gastric emptying, duodenal- gastric reflux.

The stages of disease: 1 acute condition; 2 remission.

Acute condition occurs in necrotic zone, inflammation and fibrinoid changes in the vascular walls.

Remission occurs in granulate tissue and scarring.

Grossly: Round, sharply punched –out crater of 2 to 4 cm in dia. can be observed.

Result is scar formation.

3 № 76 PHLEGMONOUS CHOLECYSTITIS H & E ***des.***

Microscopically: granulocyte infiltration of the gall bladder wall can be seen. The tissue structures are subjected to suppurative fusion. The mucous membrane is fully destroyed in some foci with ulceration.

Complication: a) perforation and peritonitis; b) empyema of the gallbladder; c) biliary cirrhosis; d) pancreatitis.

Clinical signs: Irradiation of the pain into the chest left part with imitation of myocardial infarction. Myocardial infarction can be provoked by attack of acute cholecystitis.

Result is fibrosis of the wall.

4 № 77 CHRONIC CALCULOUS CHOLECYSTITIS. H & E

Microscopically: The wall can be thin or thick with sclerosis and lymphocytes infiltration.

Grossly: The gallbladder can be contracted, of normal size or enlarged. Presence of stones within the lumen of the gall bladder can be noted.

Complications of chronic cholecystitis: a) bedsore with stone and bile peritonitis;
b) hydrocele; d) petrification of the wall; e) adhesions.

Result is deformation of the gallbladder.

5 № 263 PHLEGMONOUS ULCEROUS APPENDICITIS H & E ***des***

Microscopically: All layers of the wall are infiltrated by exudate consisting of numerous granulocytes. The tissue structures are subjected to suppurative fusion. The mucous membrane is fully destroyed in some foci with ulceration.

Grossly: appendix is red, swollen, dull, covered with a fibrinous purulent exudate of grey- yellow color.

Definition: appendicitis is inflammation of the appendix.

Etiology: a) obstruction with coprostasis and invasive of microorganisms; b) disintegration of the nervous system of the appendix; c) secondary with generalization of infectious diseases; d) coprostasis.
Result is complication with intoxication.

6 № 270 MUCOCELE H & E

Microscopically: accumulation of mucus in the appendicular lumen with thinning of the wall can be seen.

Grossly: it is the so-called "sac with mucus".
It can malinger mucous adenocarcinoma.

Result is rupture with mucous peritonitis.

Macrosamples

Gangrenous appendicitis:

Grossly: The appendix is enlarged, of gray-black color, covered with fibrinous suppurative films of grey-yellow color on the serous membrane. and secondary gangrenous matter.

Etiology for Primary appendicitis consists of: 1 thrombosis; 2 thromboembolism of the mesenteric artery of the appendix.

Etiology for Secondary appendicitis consists of 1 mesenteriolit; 2 thromboarteritis.

Result is peritonitis and intoxication.

Calculous cholecystitis

Grossly: There are gallstones with acute or chronic inflammation of the gallbladder wall.

Pathogenesis: The inflammation can be major complication of gallstones.
First gallstones may occur without inflammation of the gall bladder; only later bacterial contamination develops.

Result is empyema or dropsy of the gall bladder.

The stone in the choledoch (common bile duct)

Grossly: Bile stone is revealed in the choledoch with lumen obturation.

Complications: purulent cholangitis, abscess of the liver.

Result is obstructive [mechanical, surgical] jaundice.

Unit 21 ACUTE INFLAMMATORY DESEASES OF LUNGS: PNEUMONIAS; ACUTE DESTRUCTIVE PROCESSES IN LUNGS. ACUTE RESPIRATORY VIRAL INFECTIONS (ARVI). INFLUENZA (GRIPP). MEASLES.

Acute pneumonia is the exudative inflammation of the lungs.

Classifications are as follows:

I. Etiology: 1.1. Viral. 1.2. Bacterial. 1.3. Fungal. 1.4. Protozoa.
1.5. Physical agents. 1.6. Chemistry agents.

II. *Pathogenesis:* 2.1. Primary. 2.2. Secondary as complications of other disease

2.3 Contagious and nosocomial [hospital-acquired] pneumonia

III.Clinical-morphological forms:

3.1Lobar (crupous) pneumonia 3.2Bronchopneumonia. 3.3 Acute interstitial pneumonia (pneumonitis).

Lobar (crupous) pneumonia

Synonyms: 1.LOBAR pneumonia- the whole lobe is involved.
2. CRUPOUS (as a type OF FIBRINOUS INFLAMMATION) pneumonia.
3. PLEUROPNEUMONIA - pleura is involved.

Definition: Acute infectious allergic inflammatory disease of the lungs involving one or more lobes of the lung.

Etiology: 1, 2, 3 types Pneumococcus and Klebsiella pneumonia (rarely).

Pathogenesis: It is caused by hypersensitivity reaction induced by pneumococci and Klebsiella with immunocomplex disorders of microcirculation. Intraalveolar fibrinous exudation occurs. Consolidation of lung parenchyma is the result of the whole lobe being involved.

Stages are revealed as:

Congestions (Influx) occurs within the First day.

Microscopically: vascular congestion with serous exudate within alveolar can be seen and many bacteria occur in the alveoli.

Grossly: the affected lobe is heavy, red and boggy.

Red hepatization (2 – 3 DAYS).

Microscopically: alveolar spaces are airless, packed with red cells and fibrin.

Grossly: The lung lobe is of liver-like consistency, of red color. Pleura demonstrates a fibrinous or fibrinous-purulent exudate.

Gray hepatization (4 – 6 days).

Microscopically: The alveolar spaces are airless, packed with neutrophils and fibrin. Septal between alveoli are thickened with neutrophils in-

filtration. Vascular congestion can be seen. The pleura demonstrates fibrinous or fibrinopurulent exudates.
Grossly: The affected lobe of the lung is dry, grey and firm (the lung lobe is of liver-like consistency). Pleura is thickened, with gray fibrinous membranes on the surface.
Resolution (9 – 11 DAYS).
Exudates within the alveoli is enzymatically digested and either resorbed or expectorated, leaving the basic architecture intact.
ATYPICAL FORMS OF CRUPOUS PNEUMONIA:
1. Central. 2. Massive. 3. Total. 4. Migratory. 5. Klebsiella pneumonia.
Complications are as follows:
Pulmonary complications: 1Carnification of the lung. 2 Abscess of the lung.
3 Gangrene of the lung. 4 Empyema of the pleura.
Extra pulmonary complications:
1 Purulent mediastinitis. 2 Purulent pericarditis (infective endocarditis).
3 Purulent peritonitis. 4 Purulent arthritis. 4 Purulent meningitis (abscess of the brain).

Bronchopneumonia (local pneumonia)

Definition: bronchopneumonia (local pneumonia) is characterized by local acute inflammation amount from acinus to segment connected with acute bronchiolitis.
Etiology: 1 viral infection (influenza, parainfluenza, measles, respiratory-syncytial infection, adenoviral infection and others). 2 Bacterial infections (pneumococcus, streptococcus, staphylococcus, pseudomonas, eroginosa, escherichia coli and others). 3 Fungal infections. 4 Protozoan infections (pneumocystis). 5 Mixed infections. 6 Physical and chemistry agents (uremic, lipid, dusty, radiation pneumonia).
Morphological changes in the lung depending on the character of stimulus (etiology)
of pneumonia.
VIRAL pneumonia is usually serous or serous – hemorrhagic pneumonia (influenza). BACTERIAL pneumonia is usually purulent. Staphylococcal and Klebsiella pneumonia is characterized by considerable alveolar wall damage, leading to necrosis with abscess formation. It may lead to empyema (pus in the pleural cavity).
Classification: LOCAL PNEUMONIA may be as follows:
1 according to amount of foci inflammation:
1.1 Acinar.

1.2 Lobular.
1.3 Confluent lobular (multilobular)
1.4 Segmental.
1.5 Polysegmental.
1.6 Bilateral.
1.7 Subtotal.
2 according to pathogenesis:
2.1Aspirate.
2.2Hypostatic.
2.3Postoperative.

Complications: 1Carnification of the lung. 2 Abscess of the lung. 3 Gangrene of the lung. 4 Pleuritis.

Acute interstitial pneumonia (acute pneumonitis)

Definition: Acute interstitial pneumonia is characterized by primary acute inflammation within interstitium of respiratory regions of the lungs and within alveolar septa.

Etiology: 1Viruses: micoplasma, L. pneumophphilia, cytomegalovirus, pneumocystis carini. 2 Fungal.

Measles

Definition: Measles is a viral contagious disease with cough, sneeze, fever, and conjunctivitis and maculopapulous rash.

Etiology: measles Virus.

Complications: **false croup (**acute laryngitis and laryngotracheitis with larynx edema), bronchiolitis, local pneumonia, bronchiectatic disease, enteropathy, encephalitis and hemorrhages of the brain.

Influenza (grippe)

Definition: Influenza is an acute viral severe contagious epidemic disease.

Etiology: three serologic types of virus occur as A, B, C RNA viruses.

Action of virus includes 1 citolytic action to the respiratory epithelium, 2 immunodepressive action, 3 vasoparalitic action, 4 naturopathic action.

Classification: there are three clinic forms of influenza (mild, medium and severe)

Severe influenza consists of a) toxic form; b) influenza with pulmonale complications.

Toxic form includes hemorrhagic pneumonia, hemorrhagic syndrome, and acute hyperplasia lymphoid organs.

Complications: a) pulmonale complications (bronchiectatic disease, pneumosclerosis, local carnification, chronic obstructive emphysema); b) extra pulmonale complications (hemorrhagic, fibrinous or purulent pleuri-

tis, purulent mediastinitis, pericarditis, meningitis, purulent encephalitis, glomerulonephritis).
Causes of death: intoxication or bacterial bronchopneumonia and complications.

Microsamples
№221 Lobar (Crupous) pneumonia des. .
№212 Carnification of the lung des.
№220 Bronchopneumonia des.
№223a Pneumonia with abscesses formation see 1-st semester
№216 Measles necrotic panbronchitis des.

Macrosamples
1 Lobar (Crupous) pneumonia.
2 Purulent lymphangitis.
3 Bronchopneumonia.
4 Trachea and lung with INFLUENZA (grippe).
5 Abscess of the brain

Microsamples
№ 211 LOBAR (CRUPOUS) PNEUMONIA. H & E ***des***.
Microscopically: according to stage, referred to as grey hepatization, there is some fibrinous exudate with leukocytes and macrophages within alveolar space and capillary collapse.
Grossly: The lobe is enlarged, uniformly consolidated, and airless, of grey color. Pleura is thickened, dull, with fibrinous film on the pleura.
Results are Resorption of the exudate or Carnification of the lobe.
Possible causes of death may be 1 acute cardiac and respiratory insufficiency; 2 purulent complications see above.
Clinical signs: The onset is abrupt, with high fever and an episode of a severe shaking chill accompanied by pleuritic chest pain and a cough productive of rusty – colored purulent sputum

. №212 CARNIFICATION OF THE LUNG H & E ***des***
Microscopically: Connective tissue replaces fibrinous exudate within alveolar space.
Grossly: The lung is mottled, dense, of grey red colors.
Definition: It occurs as a type of pneumosclerosis, manifested in the appearance of the connective tissue in the lung alveoli as a result (outcome) and complication of lobar or local pneumonia.

Pathogenesis: organization of exudate develops with deficiency in granulocytes and macrophages.
Result is pulmonale failure.

№220. LOCAL PNEUMONIA (BRONCHOPNEUMONIA) H & E ***des***

Microscopically: there can be seen airless inflammative foci with focal suppurative exudate that fills the bronchi, bronchioles and adjacent alveolar spaces.
Grossly: In the lung one can see multiple airless small and large inflammative foci of dark red to gray – yellow color, protruded over cut surface, of hard consistency.
Definition: Bronchopneumonia is a disease, characterized by local inflammation of the lung resulting from an initial inflammation of the bronchi and bronchioles with extension into the adjacent alveoli.
Results are 1Resorption of the exudates and complete recovery (usually). 2 Diffuse pneumosclerosis. 3 Carnification of the lung.
Possible causes of death are as follows: 1 Purulent complication. 2 Cardiac and respiratory insufficiency.

№216 NECROTIC PANBRONCHITIS WITH MEASLES H & E ***des.***

Microscopically: The walls of the bronchi and bronchioles are necrotic with diffuse neutrophils infiltration. Their lumen is filled with necrotic detritus. This is termed as purulent necrotic panbronchitis with focus of pneumonia.
Result: This process may lead to “destructive (saccular) bronchiectasis”.

Macrosamples

Purulent lymphangitis.

Grossly: the affected lymphatic is dilated and filled with pus. There are chiefly neutrophils and monocytes. In severe cases abscess and cellulites can be observed.

Abscess of the brain.

Grossly: It is sharply demarcated, indicating its presence for some time. Purulent exudate is visible in the center of abscess. Surgical drainage is necessary to treat such lesion.

Trachea and lung with influenza (grippe).

Grossly: Trachea is covered with abundant catarrhal and hemorrhagic exudate; mucous membrane is hyperemic with multiple petechii. The

lung is enlarged, mottled, of nonuniform density and airless of grey red color. It is so-called “the large mottled lungs”.

Result is pneumosclerosis, bronchiectatic disease, and emphysema.

Unit 21 CHRONIC OBSTRUCTIVE PULMONARY DISEASES.

Chronic diffuse inflammative pulmonary diseases are divided into three groups:

1 obstructive; 2 restrictive; 3 mixed.

Chronic obstructive pulmonary diseases are diseases with airflow obstruction.

Classification: They include chronic obstructive bronchitis, chronic obstructive emphysema, bronchiectatic disease and chronic bronchiolitis.

Chronic restrictive pulmonary diseases are interstitial diseases characterized by reduced volume pulmonary parenchyma and vital capacity with respiratory dysfunction.

Morphogenesis of Chronic diffuse inflammative pulmonary diseases develops via three pathways: 1 bronchitogenic; 2 pneumonitogenic; 3 pneumoniogenic.

Chronic obstructive bronchitis

Chronic obstructive bronchitis is a disease with chronic inflammation, hyperplasia of mucus producing goblet cells and mucous glands.

Chronic obstructive bronchitis occurs as simple and obstructive.

Obstructive chronic bronchitis occurs with obstruction of peripheral bronchi with bronchiolitis to follow.

Bronchiectasis

Bronchiectasis is termed dilation of bronchus lumen.

Classification of bronchiectasis:

According to the anatomic nature of the lesion bronchiectases are divided into

2 types: Sac-like (destructive), and Cylinder-like (retention) bronchiectasis.

Etiology: The conditions that most commonly predispose to bronchiectasis include:

Bronchial obstruction. Common causes are tumors, foreign bodies, and occasional

mucous impaction. Under these conditions, the bronchiectasis is localized to the obstructed lung segment.

Bronchiectasis can also complicate atopic asthma and chronic bronchitis.

2. Congenital or hereditary conditions. For example, in 1) Cystic fibrosis, widespread severe bronchiectasis results from obstruction and infection due to the secretion of abnormally viscid mucus. 2) In immunodeficiency states, particularly immunoglobulin deficiencies, bronchiectasis tends to develop due to increased susceptibility to repeated bacterial infections. 3) Kartagener's syndrome, an autosomal recessive disorder, is frequently associated with bronchiectasis and sterility in males. Structural abnormalities of the cilia impair mucociliary clearance in the airways, leading to persistent infections, and reduce the mobility of spermatozoa.
3. Necrotizing, or suppurative, pneumonia may predispose to bronchiectasis. Sometimes it may be a sequela of childhood pneumonias complicating measles, whooping cough, and influenza.

Pathogenesis of bronchiectasis:

The pathogenesis of bronchiectasis shows two critical and interconnected processes, there are: 1) obstruction, and 2) chronic persistent infection. Either of these two processes may come first. Normal clearance mechanisms are hampered by obstruction, so secondary infection soon follows; conversely, barely chronic infection causes damage to bronchial walls, leading to weakening and dilation. For example, obstruction due to a bronchogenic carcinoma or a foreign body impairs clearance of secretions, providing fertile superimposed infection. The resultant inflammatory damage to the bronchial wall and the accumulating exudate further distend the airways, leading to irreversible dilation. Conversely, a persistent necrotizing inflammation in the bronchi or bronchioles may cause obstructive secretions, inflammation throughout the wall (with peribronchial fibrosis and scarring traction on the walls).
In the usual case mixed flora can be cultured from the involved bronchi, including staphylococci, streptococci, pneumococci, enteric organisms, anaerobic and microaerophilic bacteria, and (particularly in children) haemophilus inftuenzae and Pseudomonas aeruginosa.

Clinical course and complications: The clinical manifestations consist of severe,
persistent cough with expectoration of mucopurulent, sometimes fetid, sputum. The sputum may contain flecks of blood; frank hemoptysis can occur. Symptoms are often episodic and are precipitated by upper respiratory tract infections or the introduction of new pathogenic agents. Clubbing of the fingers may develop. In cases of severe, widespread bronchiectasis, significant obstructive ventilatory defects develop, with hypoxemia, hypercapnia, pulmonary hypertension, and (rarely) “cor pulmon-

ale.” Metastatic brain abscesses and reactive amyloidosis are other, less frequent complications of bronchiectasis.

Bronchiectasis disease is termed multiple bronchiectasis with “cor pulmonale”.

Microsamples:
№214 Chronic bronchitis accompanied by bronchiectasis des.
№222 Chronic lung abscess des.
№213 Nodular pulmonary silicosis des.
№59 Pulmonary. Anthracosis.
№317 Chronic obstructive catarrhal bronchitis.
№315 Lung in Asthma.

Macrosamples:
Bronchiectasis and pulmonary cirrhosis.
Chronic lung abscess.
Amyloidosis of the kidney see 1-st semester
Lung in Anthracosis.
Lung in Silicosis.
Cor pulmonale.

Microsamples
№214 CHRONIC BRONCHITIS ACCOMPANIED BY BRONCHIECTASIS H & E ***des***

Microscopically: Intense acute and chronic inflammatory exudate within the walls of the bronchi and bronchioles, and desquamation of lining epithelium, cause extensive areas of ulceration. Hyperplasia of mucous glands is seen. As usual, fibrosis of the bronchial walls and peribronchial fibrosis is observed. The lumen is abnormally dilated, and scarring also persists. Lining epithelium shows prominent squamous methaplasia.

Grossly: the most severe involvement is found in the distal bronchi and bronchioles. The airways are dilated to as much as 4 times their usual diameter, and on gross examination of the lung, they can involve almost the pleural surfaces.

Definition: Bronchiectasis is the permanent dilation of bronchi and bronchioles
due to destruction of the muscle and elastic supporting tissue, resulting from or associated with chronic necrotizing infections.

Complications may be pulmonale: bronchopneumonia, atelectasis, obstructive emphysema, and pneumofibrosis.

Complications may be extra pulmonale: right-side heart failure or “cor pulmonale” and amyloidosis.

№222 CHRONIC LUNG ABSCESS H & E ***des***.

Microscopically abscess appears as a suppurative infiltration accompanied by necrosis. Infiltrate is composed of numerous of neutrophils with admixture of microorganisms, and some cell debris. Suppuration is surrounded by variable amounts of granulation tissue, which contains mononuclear cells (lymphocytes, plasma cells, macrophages), and fibrous scarring, depending on the chronicity of the lesion.

Grossly, abscesses vary in diameter from few millimeters to large cavities of 5 to 6 cm, full of pus and delineated by a pyogenic membrane. Commonly, abscesses are localized in II, VI, IX, and X segments of the right or (rarely) left lung. But however, the localization and number of abscesses depend on their mode of development.

Definition: Lung abscess is a localized area of suppurative necrosis within the pulmonary parenchyma.

Etiology and pathogenesis: The causative organism may be introduced into
the lung by any of the following mechanisms:

• Aspiration of infective material from carious teeth or infected sinuses or tonsils, particularly during oral surgery, anesthesia, coma, or alcoholic intoxication and in debilitated patients with depressed cough reflexes.

• Aspiration of gastric contents, usually accompanied by infectious organisms from the pharynx.

• As a complication of acute bacterial pneumonias, particularly those caused by
S. aureus, K. pneumoniae, Pseudomonas species, and occasionally type 3 pneumo-
cocci. Mycotic infections and bronchiectasis may also lead to lung abscesses.

• Bronchial obstruction, particularly with bronchogenic carcinoma obstructing a bronchus or bronchiole. Impaired drainage, distal atelectasis, and aspiration of blood and tumor fragments all contribute to the development of abscesses. An abscess may also form within an excavated necrotic portion of a tumor.

• Septic embolism, from septic thrombophlebitis or from infective endocarditis of the right side of the heart.

• In addition, lung abscesses may result from hematogenous spread of bacteria in disseminated pyogenic infection.

• When all the above pathogenetic pathways are excluded, there are still many cases
to consider.

Clinical course and complications: of mysterious origin, referred to as primary cryptogenic lung abscesses.

As the focus of suppuration enlarges, it almost inevitably ruptures into airways. Thus, the contained exudate may be partially drained, producing an air-fluid level on radiographic examination. Occasionally, abscesses rupture into the pleural cavity and produce bronchopleural fistulas, the consequence of which are pneumothorax or empyema. Other complications arise from embolization of septic material to the brain, giving rise to meningitis or brain abscess.

The manifestations of a lung abscess are much like those of bronchiectasis and include a prominent cough that usually yields copious amounts of foul-smelling, purulent, or sanguineous sputum; occasionally hemoptysis occurs. Spiking fever and malaise are common. Clubbing of the fingers, weight loss, and anemia may occur. Infective abscesses occur in 10% to 15% of patients with bronchogenic carcinoma; thus, when a lung abscess is suspected in an older patient, underlying carcinoma must be considered. Secondary amyloidosis may develop in chronic cases.

Treatment includes antibiotic therapy and, if needed, surgical drainage. Overall, the mortality rate is in the range of 10%.

№213 NODULAR PULMONARY SILICOSIS H&E ***des***.

Microscopically: multiple nodules are observed within the lung tissue, consisting of concentric layers of hyalinized collagen surrounded by a dense capsule of more condensed collagen. Examination of the nodules by polarized microscopy reveals birefringent silica particles.

Grossly in its early stages, Silicosis is characterized by tiny, barely palpable, discrete, pale-to-blackened (if coal dust is also present) nodules in the upper zones of the lungs. As the disease progresses, these nodules may coalesce into hard, calagenous scars. Some nodules may develop central softening and cavitation as a result of superimposed tuberculosis or ischemia. The intervening lung parenchyma may be compressed or over expanded, and a honeycomb pattern may develop.

Definition: Silicosis is a lung disease caused by inhalation of crystalline silicon dioxide (silica), and usually presents, after decades of exposure, as slowly progressing, nodular, fibrosing pneumoconiosis.

Etiology and pathogenesis: Workers in a large number of occupations are at risk,

especially sand-blasters and many mine workers. Less commonly, very heavy exposure over months to a few years can result in acute silicosis, a lesion characterized by the generalized accumulation of a lipoproteinaceous material within alveoli.

Silica occurs in both crystalline and amorphous forms, hut crystalline forms (including quartz, crystobalite, and tridymite) are biologically the most active. Of these, quartz is most commonly noted in silicosis. Talc, vermiculite, and mica are examples of no crystalline silicates that are less common causes of pneumoconiosis.

After inhalation, small particles of quartz may reach the terminal airways and to cause fibrosis. Exposure to silica demonstrates a steady increase in macrophages and lymphocytes in the alveolus and interstitium. The recruited macrophages play a leading role in secreting factors leading to fibroblast proliferation and collagen production. The initial lesions tend to localize in the upper lung zones, and show prominent fibrosis.

Clinical course and complications: The disease is usually detected in routine chest radiographs performed on asymptomatic workers. The radiographs typically show a fine nodularity in the upper zones of the lung, but pulmonary function is either normal or only moderately affected.

Most patients do not develop shortness of breath until late in the course. At this time the disease may be progressive, even if the patient is no longer exposed. The disease is slow to kill, but impaired pulmonary function may severely limit activity.

Complications: Susceptibility to tuberculosis is increased, but there is no evidence that silicosis predisposes individuals to the development of bronchogenic carcinoma.

Macrosamples:

“Cor pulmonale”.

Grossly: Chronic cor pulmonale is characterized by right ventricular and often right atrial, hypertrophy; the thickness of the right ventricular wall may exceed that of the left ventricle with their chamber dilation.

Anthracosis of the lung

Grossly: linear streaks and aggregates of anthracotic pigment readily identify pulmonary lymphatics and mark the pulmonary lymph nodes. A condition sometimes referred to as centrilobular emphysema.

Silicosis of the lung

Grossly: there are multiple nodules, predominantly, in the upper zones of the lungs.

Silicotic nodules are characterized by tiny, barely palpable, discrete, and pale-to-blackened (if coal dust is also present) nodules. As disease progresses, individual nodules may coalesce into hard, callagenous scars.

Unit 22 INTESTINAL INFECTIONS. TYPHUS FEVER. SYPHILIS. POLIOMIELITIS.

Dysentery (Shigellosis)

Definition: ***Dysentery (Shigellosis***) is an acute intestine infection, showing diarrhea, Tenesmus, abdominal pains, and severe course shows hemorrhagic diarrhea, fever and high intoxication.

Etiology: Shigella dysentery, Shigella Flexneri, Shigella boydii, Shigella sonnei.

They produce exotoxin and endotoxin.

Pathogenesis: Shigella bacteria are of fecal- oral direct transmission and contaminate water and food. Shigella bacteria damage rectum, sigmoid and descending colon. They invade the large intestine according to their genome and come to the colocytes. Shigella boydii comes out of phagolyzosome to cytoplasm of the colocytes.

Destruction of the epithelium leads to erosions. There are also vasoparalitic effects.

Toxins destroy neural apparatus of the colon.

There are four stages of bacterial dysentery: 1catarrhal colitis; 2 fibrinous

(crupous or diphtheritic) colitis; 3 ulcerate colitis; 4 recovery with regeneration.

Each stage lasts one week. Dysentery caused by Shigella Flexneri, Shigella boydii, Shigella sonnei takes its easy course with catarrhal colitis.

Colon complications: Hemorrhage, perforation, peritonitis, fibrous stenosis, phlegmona of the colon.

Extra colon complications: bronchopneumonia, pyelonephritis, serous arthritis, abscess of the liver, cahexia, amyloidosis.

Possible causes of death are complications.

Typhoid fever

Definition: ***Typhoid fever*** is an acute intestine infectious disease caused by Salmonella typhi abdominalis.

Pathogenesis: Contamination occurs via alimentary pathway. Bacteria invade intestinal epithelium cells and sensibilize lymphoid tissue with

proliferation of phagocytes in the Peyer's patches, after that Salmonella typhi with blood stream comes into gall bladder where the microorganisms proliferate.
Then they come into intestine again with bile and secondary comes into the Peyer's patches. The Peyer's patches in terminal ileum become sharply delineated, in plateau-like elevation. They are termed typhoid fever granulomas. These granulomas may be within other organs.

Common changes consist of bacteriemia, typhoid maculopapular rash and numerous granulomas within the organs: liver, spleen, heart, brain, lymph nodes.

Typhoid *Local changes* occur in the wall of ileum referred to as typhoid ileitis,
in the wall of colon is called typhoid ileitis, or typhoid ileocolitis.

There are five stages of disease: 1 brain-like swelling of the Peyer's patches;
2 their necrosis; 3 ulcer formation; 4 clean ulcers; 5 healing.

General infection changes are: hyperplasia of the lymphatic tissue, reversible changes of the parenchymal organs.

Clinic atypical forms occur as 1 typhoid lungs; 3 typhoid larynx; 4 typhoid bile
ducts.

Intestinal complications: hemorrhage, ulcer perforation, peritonitis.

Extra intestinal complications: purulent perichondritis, Zenker's necrosis of the abdominal rectum muscles, osteomielitis, arthritis, typhoid sepsis, bronchopneumonia, intramuscular abscess.

Possible causes of death are complications.

Typhus fever

Epidemic typhus is of world wide character (war, famine).

Definition: Typhus fever is anthropozoonosis infective disease with skin rash,
vasculitis, and hemorrhagic syndrome.

Etiology: Rickettsii Prowazekii microorganisms cause typhus fever.

Pathogenesis: with louse feces Rickettsii Prowazekii invade the skin in scratching and then they penetrate the blood stream. Rickettsii Prowazekii enter endothelium and smooth muscular cells of the vessels. They produce endotoxins to activate kallikrein, kinins and thrombosis.

Mild and severe clinical forms occur. Mild form of disease is characterized by skin rash and slight hemorrhages. Severe form of disease is characterized by gangrenous necrosis of the nose, finger-tips, and eyelids.

There are massive hemorrhages within the brain, serous membranes, lungs and kidneys.

Possible causes of death are massive hemorrhages.

Amebic dysentery (amebiasis)

Definition: ***Amebic dysentery (amebiasis)*** is a contamination infective disease with large intestinal lesion.

Etiology: Entamoeba histolytica is protozoal parasite spread by fecal-oral contamination.

Pathogenesis: Amebae invade the crypts of colonic glands and burrow down into the submucosa. The organisms then spread laterally to create a flask-shaped ulcer.

Parasites penetrate portal vessels and embolize liver to produce solitary or multiple discrete hepatic abscesses. Occasional amebic abscesses are encountered in lung,

heart, kidneys, and brain.

Possible cause of death: intoxication of the host organism.

Microsamples.

1 № 170 Fibrinous (diphtheritic) colitis with dysentery des.
2 № 171 Dysentery with ameba des.
3 № 182 Brain –like swelling of the Peyer's patches (typhoid fever) des
4 № 187 Typhus fever granulomas within medulla
5 № 234 Syphilitic mesaortitis

Macrosamples.

1 Typhoid fever (changes of the lymphatic follicles in the small intestine)
2 Fibrinous (diphtheritic) colitis with dysentery
3 Abscess of the liver
4 Syphilitic aneurism of the aorta
5 Solitary gumma of the liver (syphilis)
6 Hyperplasia of the spleen
7 Gangrenous necrosis of the foot, see 1-st semester

Microsamples.

1 №170 Fibrinous (diphtheritic) colitis with dysentery H&E **des.**

Microscopically: one can see deep necrosis of the large intestine wall with fibrin

and neutrophils infiltration. It is diphtheritic colitis. Nervous plexus is of reversible

and necrotic changes. Surrounding tissue shows edema and hemorrhages. Ulcers
are very deep.

Grossly: Fibrinous exudate first patchily then diffusely covers the mucosa and produces a dirty gray skin-like film or pseudo membrane. There are ulcers of whimsical forms and yellow bottom.

Result is complete regeneration or rare scar formation.

Causes of death are the complications.

Clinical signs: diarrhea, tenesmus, abdominal [visceral] pains, in severe course hemorrhagic diarrhea, fever, intoxication can be encountered

2 № 171 Purulent colitis with amebic Dysentery (AMEBIASIS) H& E **des.**

Microscopically: ulcers contain some host inflammatory cells and areas of extensive liquefactive necrosis. Amebae can mimic macrophages.

Grossly: the cecum and ascending colon are mostly involved. There are numerous
flask- shaped ulcers with a narrow neck and a broad base.

Definition: Amebic dysentery (amebiasis) is the intestinal infection disease caused by Entamoeba histolytica with purulent colitis.

Intestinal complications: 1 perforation; 2 peritonitis; 3 healing with scarring and
stenosis.

Causes of death are intoxication and insufficiency of the organs can be involved.

3 № 182 BRAIN –LIKE SWELLING OF THE PEYER'S PATCHES (TYPHOID FEVER) H& E **des.**

Microscopically: a some lymphocytes and multiple monocytes and macrophages form typhoid granulomas. This is an acute productive inflammation with the formation of typhoid granulomas, reflecting type 1Y hypersensitivity (cell-mediated) reaction.

Grossly: aggregated lymphatic follicles (Peyer's patches) are enlarged swelling with blood congestion and rough surface called brain-like. One can see their development within ileum (small intestine).

Definition: Typhoid fever is an infection disease caused by Salmonella typhi with damage of terminal ileum.

The stage of Peyer's patches changes is the first one as brain-like swelling;

Result is the second stage of necrosis.

4№ 187 Typhus fever granulomas within medulla H& E

Microscopically: the small vessels lesions include underlie focal areas of hemorrhage and productive vascular inflammation.

There are cuffs of inflammatory mixed leukocytes surrounding the involved vessels. The vessels include vascular thrombi leading to the gangrenous necrosis.

In the brain characteristic typhus nodules are composed by focal microglial proliferation mixed with leukocytes as typhus granulomas.

Grossly: skin rash, hemorrhages; necrosis of the organs.

Definition: typhus fever is an infection disease caused by Rickettsii Prowazekii

Complication: hemorrhage and necrosis.

Causes of death are complications.

5 № 234 Syphilitic mesaortitis H& E.

Microscopically: the gummous infiltrate consists of lymphocytes, plasmacytes, epithelioid cells with capillary-like vessels. The inflammation involves the *vasa vasorum* and destruction of the elastic fibers.

Grossly: the aortic intimae become rough, wrinkled, with multiple scar contractions called “barky- tree” or “shagreen”. Inflammation is confined to the thoracic aorta involving the arch and ascending parts of aorta.

Tertiary syphilis with syphilitic mesaortitis can be noted.

Etiology: trepanema pallidum.

The result is syphilitic (luetic) aneurysm.

Complications: rupture of aneurism with hemopericardium is affected in some cases.

The causes of death are complications.

Macrosamples

Syphilitic aneurism of the aorta

Grossly: ascending aorta with dilation of the aortic root and arch is observed.

Definition: aneurysm is a localized abnormal dilation of a blood vessel or the heart.

Etiology: trepanema pallidum.

Syphilitic aneurism of the aorta is a complication of syphilitic mesaortitis

Complications: rupture of aneurism with hemopericardium is affected in some cases.

Solitary gumma of the liver (syphilis)

The form of tertiary syphilis is the so-called benign tertiary syphilis, characterized by the development of gummas in various sites including the liver.

Spirochetes are rarely visible within the lesion.

Grossly: Gumma is an irregular, firm mass of necrotic tissue surrounded by resilient connective tissue.

Microscopically: gumma contains a central zone of coagulation necrosis surrounded by a mixed inflammatory infiltrate composed of lymphocytes, plasma cells, epithelioid cells and peripheral small vessels.

Hyperplasia of the spleen

Grossly: the spleen is enlarged, weighing between 300 and 500 g.

There is hyperplasia of white and red pulps is observed.

Unit 23 SEPSIS AND MENINGOCCOSIS.

Sepsis

Definition: Sepsis is a polyetiologic, non contagious disease characterized by generalized [systemic] infection, acyclic clinical course, and special significance of changed reactivity.

Etiology: Staphylococcus, streptococcus, esherichia coli, blue pus bacillus, proteus,

klebsiella, Gram negative bacteria and fungi.

Classification depends on entry of infection:

1 therapeutic sepsis; 2 surgical sepsis; 3 gynecologic sepsis; 4 umbilical sepsis;

5 tonsilogenic sepsis; 6 odontogenic sepsis; 7 otogenic sepsis; 8 urogenic sepsis;

9 cryptogenic sepsis (without entry of infection).

Four forms of sepsis course occur: 1fulminant (1 day); 2 acutissimus (1-3 days);

3 acute (2-3 weeks); 4 lingering (more than 3 weeks).

There are four clinical – morphologic forms of sepsis: 1 septic pyemia;

2 septicemia; 3 septic (bacterial) endocarditis; 4 chroniosepsis.

Septic pyemia is a form of sepsis with microbial embolism into the organs and multiple abscesses within the organs.

Pathogenesis: entry of infection and the septic primary focus produce thrombophlebitis, then lymphangitis and lymphadenitis with multiple abscesses within the organs to follow.

Complications are revealed by pleural empyema, purulent peritonitis, purulent
paranephritis and acute septic polypous ulcerous endocarditis.

Acute septic Polypous ulcerous endocarditis may develop during septic pyemia with pus on the valvular endocardium of the heart. This pus shows acute septic endocarditis as a part of septic pyemia as that from the clinical morphologic form of sepsis, i.e. septic (bacterial) endocarditis.
Possible causes of death are complications.

Septicemia *is the form* with hypereaction of the organism with DIC-syndrome,
Jaundice, hemorrhagic diathesis, necrosis of the organs, reversible injury of the organs. Bacterii are in the blood stream. The spleen called "septic spleen" may weigh 500gr and even 1500gr. with myeloid methaplasia.
Septicemia is considered to be a toxic infectious Shock. Clinical course may occur as fulminant or acute. Patients die within 1 to3 days.

Possible causes of death are intoxication and multiple organ failures.

Septic (bacterial) endocarditis is the form of sepsis when cardiac valve is used for entry of infection. Septic focus is localized on valvular leaflets.

Rheumatic, brucellous, syphilitic, atherosclerotic valvular diseases and heart malformation may take priority over septic endocarditis, termed secondary septic (bacterial) endocarditis. Primary septic endocarditis develops on intact valvular leaflets termed Tchernogubov's disease.

Course of disease may occur as 1 acute form; 2 subacute form and
3 chronic form termed lingering septic endocarditis or *sepsis lenta.*

Pathogenesis of septic endocarditis is connected with blood circulation of immune complex formed of antigens, antibodies, and compliment with lesions of valves, vessels, kidneys and spleen.
Thromboembolic syndrome may develop as a complication.
Possible cause of death may be complications.
Modern conception of chroniosepsis.

Chroniosepsis is characterized by primary purulent focus organ atrophy, cahexia

Causes of death are cahexia, amyloidosis and other diseases.

Purulent-absorption fever is termed by I.V. Davidovsky. Clinical presentations and pathological manifestations of local purulent and necrotic processes with demarcate border. Modern term is intoxication or endotoxicosis.

Meningococcosis

Definition: ***Meningococcosis*** is an infective disease in three forms:

1 acute nasopharingitis; 2 purulent leptomeningitis; 3 meningococcemia.

Etiology: Nesseria meningitidis.

Pathogenesis: Meningococcosis is a respiratory infection and Nesseria meningitidis can overcome hemato-encephalic barrier. The entries of infection are mucous membranes of the nose and the fauces.

Acute nasopharingitis develops in a mild clinical course.

Leptomeningitis is an inflammation of pia mater of the brain, and arachnoid of the brain.

Leptomeningitis is characterized by four clinical courses: 1 fulminant, 2 acute, 3 subacute, 4 chronic. *Leptomeningitis occurs as spinal and craniocerebral.*

Complications: purulent meningoencephalitis, thrombophlebitis, hemorrhagic infarction of the brain, fibrous adhesions and hydrocephalus.

Meningococcemia develops in a clinical course as meningococcal sepsis and manifested in DIC- syndrome, hemorrhagic diathesis, and necrosis of the organs.

Severe course may take a fulminant form.

Sometimes fulminant form reveals hemorrhage within bilateral adrenal with acute adrenal insufficiency, described as Waterhouse –Friderichsen syndrome.

The syndrome may be the cause of death.

Microsamples

1 № 94 Phlegmon with septic thrombophlebitis of the subcutaneous fat des

2 № 90 Acute pyogenic (meningococcal) meningitis des

3 № 180 Polypous – ulcerous endocarditis (endocarditis polypoulcerosa) des

4 № 91 Embolic (metastatic) abscesses of the kidney see 1-st semester

Macrosamples

1 Purulent endometriitis (puerperal endometriitis) see 1semester

2 Embolic abscesses of the kidney see 1semester

3 Polypous – ulcerous endocarditis (endocarditis polypoulcerosa)

4 “Large mottled kidneys”

5 Hyperplasia of the spleen

6 Hemorrhagic diathesis see 1-st semester

7 Pyogenic (bacterial) meningitis (of the brain or the spinal cord)

8 Hemorrhage within the adrenal

Microsamples

1 № 94 PHLEGMONON WITH SEPTIC THROMBOPHLEBITIS OF THE SUBCUTANEOUS FAT H & E ***des***

Microscopically: Diffuse neutrophilic infiltration of the subcutaneous fat as
phlegmon with a development of the purulent thrombophlebitis.

Grossly: The zone of purulent inflammation may be enlarged, tumor-like,
Red colored, feverish, causing pain.
This is an entry of infection and it can be a primary focus.
Sometimes the septic primary focus can locate far from an entry of infection.

Possible result is sepsis.

2 № 180 POLYPOUS – ULCEROUS ENDOCARDITIS (ENDOCARDITIS POLYPOULCEROSA***)*** H&E ***des.***

Microscopically: One can see colonies of microorganisms, necrosis and ulceration of the leaflets with lympho-hystiocytic and macrophageal infiltration without neutrophils (pus).

Grossly: there are massive thrombotic impositions on the valvular surface like polyps. They easily crumble, and can be classificated and organized. These processes lead to valve diseases.
Polypous – ulcerous endocarditis may be primary occurring on the healthy leaflets as Tchernogubov's disease and may be secondary on impaired leaflets by syphilis, rheumatic disease, atherosclerosis etc.

Result is valve disease.

Complications: thromboembolism with multiple infarcts within the organs without purulent inflammation.

Classification: 1 acute; 2 subacute; 3 chronic.
Chronic septic (bacterial) is as "sepsis lenta".

Causes of death are 1intoxication; 2 acute heart failure; 3 chronic heart failure;
4 polyorgan insufficiency.

3 № 90 ACUTE PYOGENIC (MENINGOCOCCAL) MENINGITIS H & E ***des.***

Microscopically: subarachnoid space is filled with neutrophils in severely affected areas and they are found predominantly around the leptomeningeal blood vessels in less severe cases.

Grossly: normally clear, cerebral spinal fluid is cloudy and sometimes frankly
purulent. The exudate is evident within the leptomeninges over the surface of the brain. The meningeal vessels are engorged and stand out prominent.

Pyogenic meningitis is caused by *Nesseria meningitidis.*

Results are 1 complete resorption; 2 organization with leptomeningeal fibrosis and consequently hydrocephalus.

The complications of acute pyogenic meningitis are*:* 1 encephalitis; 2 pyocephalus.

Causes of death may be: 1edema of the brain; 2 intoxication; 3 hydrocephalus.

Macrosamples

Hemorrhage within the adrenal

Grossly: severe adrenal hemorrhage

Caused by septicemia or meningococcemia with overwhelming sepsis.

Waterhouse-Friderichsen syndrome

Clinical sign is an acute adrenal insufficiency, that cause death

"Large mottled kidneys" (glomerulonephritis)

Grossly: the kidney is enlarged, with a smooth surface and petechii.

Etiology: Streptococcus, staphylococcus with formation of immune complexes.

Disease is a septic (bacterial) endocarditis.

Hyperplasia of the spleen

Grossly: The spleen is enlarged due to myeloid methaplasia with atrophy of lymphoid follicles.

Etiology: Microbial toxins.

Disease is termed sepsis.

Unit 23 TUBERCULOSIS.

Definition: Tuberculosis is a chronic infectious disease caused by Mycobacterium tuberculosis, characterized by involving of the lungs but may affect any organ

or tissue in the body.

Course of tuberculosis is as follows: exudative inflammation and caseous necrosis during acute phase and proliferative inflammation with specific granulomas formation and fibrosis during chronic phase.

Classification: Principally tuberculosis is divided into 3 main clinical-morphologic types: 1Primary tuberculosis develops as a result of primary infection and appears as a primary tuberculous complex (Ghon complex), 2 Hematogenous tuberculosis, and 3 Secondary tuberculosis

Etiology: Tuberculosis is a mycobacterium infectious disease. There are a lot of

types of Mycobacterium, but only 3 of them are a human pathogens.

They are Mycobacterium tuberculosis, Mycobacterium bovis, and Mycobacterium africanum, included in the Mycobacterium tuberculosis complex. These organisms are the etiologic agents of human tuberculosis.

There are two pathways for infection to follow: 1 aerogenic; 2 alimentary.

Pathogenesis: Immunity to a tubercular infection is primarily mediated by T cells and is characterized by development of hypersensitivity and resistance to the organism.

The chief implications of primary tuberculosis are 1) it induces hypersensitivity and increased resistance; 2) the foci of scarring may harbor viable bacilli for years, perhaps life long, and thus, be a site for reactivation later when host defenses are compromised; and 3) uncommonly, the disease may develop without interruption into the so-called progressive primary tuberculosis or disseminated disease.

The process of primary tuberculosis development begins in the primary lung focus (Ghon focus) with elimination of surrounding inflammation. Proliferation replaces exudation. The rim of epithelioid and lymphoid cells, appears around the focus of caseative pneumonia. Outside the rim numerous of tubercles appear. So, the primary focus undergoes encapsulation.

Outcome: The process represents an outcome of the primary tuberculosis, persisting life long.

Morphologic appearance: Aerogenic contamination leads to primary tuberculosis complex (Ghon complex) within the lung, consisting of three parts.

1 Primary focus or affection occurs within the right lung under pleura,

in 3, 8, 9, 10 segments. Primary focus (Ghon focus) consists of caseous

necrosis with serous-fibrinous pleuritis. 2 Tubercular lymphangitis includes

lymphostasis and tubercular granulomas within perivascular tissue.

3 Lymphadenitis of bronchipulmonal, bronchial and byfurcar lymph nodes.

Alimentary contamination leads to primary tuberculosis complex within the small intestine, this consists of three parts. 1 Primary focus (affection) occurs as ulcer of the intestinal wall. 2 Tubercular lymphangitis. 3 Lymphadenitis of mesenteric lymph nodes.

Clinical course of primary tuberculosis includes three variants: 1 primary tuberculosis loss with healing of primary tuberculosis complex; 2 progressive primary tuberculosis with process of generalization; 3 chronic primary tuberculosis.

Progress of primary tuberculosis may spread to: 1 lymphogenic pathway; 2 hematogenic pathway; 3 growth of primary affect; 4mixed.

Hematogenic tuberculosis is characterized by predominance of productive tissue reaction, hematogenic generalization, lesion of various tissues.

There are three types of hematogenic tuberculosis: 1 generalized tuberculosis; 2 hematogenic tuberculosis with predominant pulmonary lesion; 3 hematogenic tuberculosis with predominant extra pulmonary lesion.

1 *generalized tuberculosis includes* three forms: 1.1 fulminant Tuberculous Sepsis;

1.2 acute common miliary tuberculosis; 1.3 acute common large local Tuberculosis; 1.4 chronic common miliary tuberculosis.

2 hematogenic tuberculosis with predominant pulmonary lesion includes: 2.1 acute and chronic miliary tuberculosis of the lungs; 2.2 hematogenic disseminated large local tuberculosis of the lungs.

3 hematogenic tuberculosis with predominant extra pulmonary lesion includes:

3.1 bone- joint form; 3.2 urinary- infiltrative tuberculosis genital form; 3.3 tuberculous meningitis; 3.4 skin form.

Secondary tuberculosis consists of high morphologic forms, to extend along several different forms called stages.

1 *acute local tuberculosis* (foci of Abricosov's reinfection) occurs in 1, 2 segments of right (rare left) lung as caseous pneumonia. Healing with encapsulated petrification is termed Aschoff-Pule foci;

2 *fibrous- local tuberculosis* includes foci of healing and acute condition;

3 *infiltrative tuberculosis* (Assman-Redecker foci) consists of small Focus of caseous necrosis with perifocal serous exudate and cellular infiltration;

4 *tuberculema* is encapsulated focus of caseous necrosis of 5cm in dia.;

5 *caseous pneumonia* is characterized by massive caseous necrosis.

6 *acute cavernous tuberculosis* develops with cavity formation within caseous masses. Cavity of 2-7cm in dm is formed in 1-2 segments of the lungs connected with bronchus.

7 fibrous-cavernous tuberculosis (pulmonary consumption) includes chronic cavity, pneumosclerosis, petrification, foci of caseous pneumonia;

8 *cirrhotic tuberculosis* is characterized by scar formation, local-diffused pneumosclerosis and bronchiectasis.

Microsamples:

№241 The Ghon focus (Ranke complex) of scarring des

№242 Caseous pneumonia (Predominance of exudative reaction) des.

№244 Miliary tuberculosis of the lung des

№249 Meningeal miliary tuberculosis (Tuberculous meningitis).

Macrosamples:

The Ghon focus (Ranke complex)

Primary Tuberculous complex (The Ghon complex), see above.

Fibrinous pericarditis, see 1-st semester

Systemic miliary tuberculosis (lung, spleen, liver).

Isolated-organ tuberculosis (kidney, uterus, vertebral column).

Amyloidosis of the kidney, see 1-st semester

Fibrous-cavernous tuberculosis

Microsamples

1 №241The Ghon focus (Ranke complex) underwent scarring H & E ***des.***

Microscopically: there is a focus of encapsulated caseous masses within the lung tissue. Caseous masses may show petrification, sometimes prominent. Capsule is composed of fibrous tissue, containing blood vessels in exter-

nal layers and some giant cells in internal layers. Within some period of time caseous masses develop metaplastic ossification.

Grossly: a 1- to 1.5 cm area of grey- white focus of stony density is usually localized under the pleura in the lower part of the upper lobe.
Changes described beyond represent an outcome of the primary tuberculosis.

Clinical correlations:
Petrified foci are usually observed in healthy people: in 6% of autopsied children up to 10 years old; in 45% of young adult autopsies (20 to 30 years old), and almost 100% of over 40 years old persons autopsies.
The host-to-agent contact may lead not only to disease, but also may cause infection without clinically significant tissue damage. Such infection induces hypersensitivity and increased resistance. Anti-tuberculosis immunity is infectious, or non-sterile, i.e. it is possible only with viable organisms persisting in the latent focus of infection. *Healed Ghon* focus may represent source of latent infection. But reactivation of dormant primary lesions may also give rise to a postprimary disease.

2 №242 Caseous pneumonia (Predominance of exudative reaction) H & E ***des.***

Microscopically: Confluent massive foci of exudative inflammation occur within the lung. Alveolar exudate includes serous fluid, fibrin, leukocytes and lymphocytes. Caseous necrosis can be seen in the center of inflammatory focus. Pulmonary structure is not revealed (vague lung marking of violet color as kariorrhexis is noted).

Grossly: the lung is enlarged, firm, with prominent amounts of fibrin, covering pleura. The cross-section is yellow-grey colored. *The process may show acinar component to lobar affect.*

Definition: changes described beyond represent a manifestation of secondary lung tuberculosis. Secondary tuberculosis is the pattern of the disease arising in a previously sensitized host from reactivation of dormant primary lesions or exogenous re-
infection.

Pathogenesis: Secondary pulmonary tuberculosis is classically localized of the apex of one or both upper lobes. The reason is obscure but may be related to high oxygen tension in the apices. Due to preexistence of hypersensitivity, the bacilli produce a prompt and marked tissue response that tends to approach the wall of the focus. Cavitation occurs readily in the secondary form, resulting in dissemination along the air-

ways. Erosion into an airway becomes an important source of infectivity because the patient now produces sputum containing bacilli.

Complications in secondary tuberculosis are usually connected with cavitation and

represent *bleeding* (hemoptysis), pneumothorax, purulent pleuritis (empyema of

pleura). *Amyloidosis* may also complicate the disease as a result to prolonged pro-

cess. Rarely, in the terminal stages of the disease, hematogenous dissemination may

take place with *meningitis* development, especially in marked immunodeficient per-

sons. Sometimes extra pulmonary isolated organ tuberculosis may occur.

Possible causes of death: lung and heart failure, bleeding, amyloidosis with uremia.

3№244 MILIARY TUBERCULOSIS OF THE LUNG H & E ***des.***

Microscopically: multiple small nodules are seen within the lung tissue composed of central caseation, surrounded by the rim of epithelioid cells with admixture of some Pirogov-Langhans giant cells. Peripherally a thin rim of lymphoid cells is present.

Grossly: the lung is slightly enlarged, soft, with disseminated miliary (millet-like) gray-white to yellow colored granulomas, not more than 2 mm in diameter.

Pathogenesis: Miliary lung tuberculosis results as follows:

1 Progressive primary tuberculosis in the cases of hematogenous generalization from the Ghon focus,

2 Hematogenous tuberculosis in the cases of reactivation in the foci of scarring (healed Ghon foci) when the host defense is compromised.

3 In very rare cases secondary tuberculosis may develop a miliary disease as a result of intracanalicular or hematogenous spread in weakened persons.

Outcome: Outcome of tuberculous granulomas depends on immunologic status of the host and may show 1) total necrosis in immunodeficient patients, or 2) fibrosis in sufficient immunity.

4 №249 MENINGEAL MILIARY TUBERCULOSIS (TUBERCULOUS MENINGITIS) H & E.

Microscopically: serous- fibrinous exudate is revealed with caseous necrosis and lymphocytes and leukocytes set. Cranial arachnoid and choroids contain tubercles.

Grossly: Exudate is caseous or jelly-like and can be seen in a cistern closed to spinal cord.

Pathogenesis: Mycobacterium tuberculosis spreads to subarachnoid space via he-

matogenic pathway with miliary semination or circulation from tuberculous focus.

Complications: there are small infarcts of the brain and hydrocephalus.

Result is meningeal adhesitions.

Macrosamples:

Systemic miliary tuberculosis of the lung, spleen, liver.

Grossly: Multiple grey- white tubercles granulomas can be seen within organs.

Definition: Hematogenous tuberculosis is evident.

Pathogenesis: Infective foci in the lungs seeding in the pulmonary venous return to the heart. Organisms disseminate through the systemic arterial system. Every organ in the body can be seeded. Lesions resemble those of the lung. Miliary tuberculosis is most prominent in the lung, spleen, liver and other organs.

Isolated-organ tuberculosis of the kidney, uterus, vertebral column.

Grossly: Organs typically involved include the kidney (renal tuberculosis), uterus

(genital tuberculosis), vertebral column (osteomielitis) called Pott disease.

Pathogenesis: isolated –organ tuberculosis may occur in one of the 5 organs seeded

hematogenously.

Unit 24 ACQUIRED IMMUNODEFICIENCY SYNDROME (AIDS) (HIV –INFECTION)

Definition: AIDS is a retroviral disease caused by the human immunodeficiency virus (HIV) and is characterized by profound immunosuppression leading to opportunistic Infection, secondary neoplasms and neurologic manifestation.

AIDS represents the fifth most common cause of death in adults between the ages of 25 and 44.

Epidemiology: transmission of HIV occurs with blood or body fluids containing the virus or virus-infected cells.

The largest groups of infected individuals are homosexual or bisexual males;

intravenous drugs abusers are another group involved.

Recipients of blood and blood components;

Hemophiliacs;

Heterosexual contacts;

Infected mothers and their newborns are high-risk group.

Etiology: there are HIV-1 and HIV-2, which primarily affect CD+4 T-cells,

helper T –cells, macrophages, monocytes and dendric cells.

Pathogenesis: Loss of CD 4+ T-cells occurs due to increased destruction and reduced production. HIV-infected macrophages are found in the tissues and not in the

peripheral blood.

AIDS Course consists of three phases: 1early (acute) phase; 2 middle (chronic) phase; 3 final (crisis) phase.

1 **early (acute) phase** represents the initial response of an immunocompetent adult

to HIV infection. Clinically, there is a self limited illness characterized by nonspecific symptoms including sore throat, myalgia, fever, rash and sometimes aseptic

meningitis. There is a high level of virus production, viremia, and seeding of the peripheral lymphoid tissues. Infection is controlled by antivirus immune response.

2 **middle (chronic) phase** represents a stage of relative containment of the virus,

The immune system is largely intact at this phase. There is a continuous HIV replication within several years. *Persistent lymphadenopathy* with significant constitutional symptoms (fever, rash, fatigue) reflects the onset of immune system decompensation.

3 ***final (crisis) phase*** is characterized by *a catastrophic breakdown of host defenses*, a marked increase in viremia and clinical disease (fever, fatigue, weight loss

and diarrhea. After a variable interval (several years) patients develop serious opportunistic infections, secondary neoplasms and neurologic manifestations.

The most common opportunistic infections are:
Protozoal and Helmintic, such as:
Cryptosporidiosis,
Pneumocystosis,
Toxoplasmosis,
Fungal infections, including:
Candidacies,
Cryptococcus,
Coccidioidomycosis,
Histoplasmosis,
Bacterial infections, such as:
Mycobacteriosis, including Tuberculosis,
Salmonella-infections,
Viral infections, especially:
Cytomegalovirus,
Herpes virus.

The tumors, which are characteristic for HIV-infection, are also opportunistic, as they are associated with viruses:
Kaposi's sarcoma, associated with Cytomegalovirus,
Burkett's lymphoma, associated with Epstein-Barr virus.

Nowadays 3 types of AIDS are distinguished:
1AIDS accompanied by opportunistic infections and tumors.
2 AIDS-associated complex characterized by absence of clinically significant manifestation.
3 Persistent generalized lymphadenopathy affecting more than 2 groups of lymph nodes within more than 3 months period.

Clinical syndromes, which may be encountered in HIV-infected persons:
Lung syndrome,
Neurological syndrome,
Intestinal syndrome,
Damage of the skin and mucous membranes,
Lymphadenopathy,
Fever,
Retinopathy.

The lung syndrome represents fever and cough accompanied by poor auscultative symptoms. Most commonly, Pneumocystis Carinii Pneumonia, Cytomegalovirus infection, Mycobacteriosis and Toxoplasmosis are etiologic factors. Pneumonia caused by Pneumocystis Carinii is the most common opportunistic infection in AIDS, affecting more than 85% of pa-

tients. It is characterized by eosinophilic exudation within alveoli, accompanied by cell proliferation and diffuse interstitial lung fibrosis.

Cytomegalovirus infection is one of the most common generalized infections in AIDS. Diagnosis is based on large cells containing intranuclear inclusions which found in diffusely disseminated lung tissue.

Neurological syndrome can be found as in Meningoencephalitis caused by Cytomegalovirus, Herpes virus, Candida, Cryptococcus, Toxoplasmosis.

Intestinal syndrome is characterized by diarrhea and exhaustion caused by Shigella, Campylobacter, Cryptosporidium, Clostridia.

Neoplasms are most common in AIDS:

Kaposi's sarcoma,

Non-Hodgkin's lymphomas (Burkett's lymphoma),

Primary lymphoma of the brain,

Invasive cancer of the uterine cervix.

Microsamples:

1 № 307 Cytomegalovirus sialadenitis **des.**

2 № 96 Actinomycosis of the tongue **des**

3 № 122 Mucormycosis of the lung **des**

4 № 318 Kaposi's sarcoma **des.**

Microsamples:

№ 307 CYTOMEGALOVIRUS SIALADENITIS H & E **des**.

Microscopically: In the glandular organ, the parenchymal epithelial cells are affected. Epithelial cells of Salivary gland ducts are strikingly enlarged and show huge nuclei surrounded by a light border. These cells are the so-called "owl's eye".

Lymphoid infiltration can be seen within interstitial tissue.

№ 96 ACTINOMYCOSIS OF THE TONGUE **des**

Microscopically: Multiple actinomycotic granulomas can be seen within tongue tissues. They consist of abscesses with pink or violet druses of Actinomycetales.

Granulation tissue with predominance of xanthome cells surrounds abscesses.

№ 122 MUCORMYCOSIS OF THE LUNG **des**

Microscopically: Enlarged locations of necrosis and suppuration can be seen within pulmonary tissue. Nonseptate hyphae with obtuse– angle branching occur.
There are marked disorders of the blood stream.

№ 318 KAPOSI'S SARCOMA **des.**
Grossly: Three forms can be identified: patches, raised plaques and nodular.
Patches are pink to red and purple with solitary or multiple macules usually confined to the distal lower extremities.
Microscopically: Multiple vascular spaces with thinner walls and lined with plump spindle cells and well differentiated endothelium. Hemorrhages and hemosiderin can be seen within areolar stroma.

Suggested Text-books and manuals to be studied:

1 V.Kumar, R.S. Kotran, S.L.Robbins. Robbins Basic Pathology. 7-th edition.
Sunders Company. 2003: 873.

2 V. Kumar, A.K. Abbas, N. Fansko. Robbins & Cotran. Pathologic Basis of Disease. 7-th edition. Sunders Company. 2004:1552

3 R. Reid, F. Roberts. Pathology illustrated. Churchill Livingstone. 2005: 692

4 P. Boss, S. Burroughs, C.Way. Master Medicine: Systemic Pathology. Churchill Livingstone. 2005: 232

5 М.А. Пальцев, Н.М. Аничков, М.Г. Рыбакова. Руководство к практическим
занятиям по патологической анатомии.- М: Медицина. 2002: 892

О.П. Шевченко, О.Д. Мишнев. Атлас ишемической болезни сердца.
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